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Monthly Message

We have recently received the first annual report from the Toxicological Information Center. The armed services have a particular interest in this Center because approximately two years ago Dr. Harold C. Hodge, the Chairman, met with our Civilian Advisory Council and recommended its establishment. This office explored the possibilities with the National Research Council and it was agreed that such a center should be established within the Division of Chemistry and Chemical Technology. With the rapid development of new chemical compounds such as solvents, lubricants, plastics, vapor, gases and fuels, insecticides and pesticides, such a center becomes extremely important. It acts as a clearing house and index catalogue for the work in toxicology being performed by the various government agencies and industry, and so performs an extremely valuable function in assuring that such information may be available to any qualified person or group at any time.

We are extremely happy to welcome this Center and endorse the work it is doing. It is the only agency of this nature, and hence its work will become of increasing importance in the years ahead.

Frank B. Berry

FRANK B. BERRY, M. D.
Assistant Secretary of Defense
(Health and Medical)

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Foreword

The *United States Armed Forces Medical Journal* is the medium for disseminating information of administrative and professional interest to all medical personnel of the Department of Defense. The Assistant Secretary of Defense (Health and Medical) and the Surgeons General of the several services invite all medical officers, dental officers, Medical Service Corps officers, Nurse Corps officers, and officers of the Veterinary Corps of the Armed Forces, and the medical consultants of the Army, Navy, and Air Force to submit manuscripts for publication in this *Journal.*

FRANK B. BERRY, M. D.,
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MAJOR GENERAL SILAS B. HAYS,
Surgeon General, United States Army.

REAR ADMIRAL BARTHOLOMEW W. HOGAN,
Surgeon General, United States Navy.

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Surgeon General, United States Air Force.

UNITED STATES ARMED FORCES
MEDICAL JOURNAL

Volume IX May 1958 Number 5

JET INJECTION LOCAL ANESTHESIA IN DENTISTRY

A Report of 66 Cases

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JET INJECTION is the term given to the principle of injecting fluids into the skin and mucous membranes by forcing liquid substances through very small openings or jets at very high pressure. The velocity, depth of penetration, and spread depend on the size of the orifice, spring pressure, and type of fluid as well as the type and location of tissue being injected.[1] One of the unique features of this method is the ability of the very fine column of liquid, traveling at speeds of approximately 700 feet per second, to pierce the tissues without eliciting a pain response, or at the most, causing only very slight pain.

In 1947 Hingson and Hughes,[1] using jet injection, reported the administration of 0.25 ml of 2 per cent procaine with 1: 25,000 epinephrine at a pressure of 3,500 pounds per square inch (p. s. i.), to anesthetize the skin of patients preparatory to performing either caudal or spinal analgesia. In 1951 Krohn, Spriggs, and Dabbs[2] injected 29 male patients undergoing anal surgery with 0.25 ml of 4 per cent Xylocaine (brand of lidocaine hydrochloride) in almond oil. Sites of injection were inspected daily throughout their hospital stay and at three weeks after discharge from the hospital. There was no evidence of edema,

From Research and Development Division, Office of the Surgeon General, Department of the Army.

erythema, induration, abscess, or sloughing. It was shown that these 29 patients exhibited much less postoperative discomfort than a comparable control group.

Hingson[3] reported that on a basis of 5,000 patients he did not believe that inadvertent intravenous injection was as likely with jet injection as it was with the needle and syringe method. He further stated that he was convinced, by both clinical and histologic study of tissue, that there was less trauma with jet injection than with the needle and syringe.

Although the administration of drugs and local anesthetics by means of jet injection in many areas of the body has been reported in the literature,[1-6] there has been no report of its use in dentistry. The object of this investigation was to determine the feasibility of producing local anesthesia of sufficient depth and duration, utilizing the jet injection principle, to allow the completion of such routine dental procedures as cavity preparation and the extraction of teeth.

METHODS

The injectors used were single-shot, hand-operated, spring-loaded instruments for parenteral injection of medications in calibrated volumes of 1 ml or less.* They are 21 cm in length and 4 cm in diameter. The jet injector is an interconnected, two-part mechanism, the front part containing the metal ampule of material to be injected (Metapule), and the back part, the power source (fig. 1). The only modification of the above instrument for this work was to extend the tip to a length of 2 inches (fig. 2).

The power source is a spring-activated plunger. On the power stroke, the plunger contacts the stopper at the rear of the Metapule with sufficient force to drive the solution ahead of the stopper through the orifice of the Metapule.

The injector contains six springs which are energized by compression through a screw and nut principle (fig. 3). The instantaneous release of the spring energy is accomplished by depressing a latch release button.

By reason of high spring pressure and small plunger diameter an instantaneous pressure of 16,000 p. s. i. is developed within the Metapule. As the fluid is expressed from the Metapule, the pressure drops to approximately 7,000 p. s. i. and then tapers off to 3,000 p. s. i., at the end of the shot as the springs expand and lose energy.** Due to the nature of the tissue and the second-

*The injectors used in these tests were made available on a loan basis by R. P. Scherer Corp. Detroit, Mich.

**Personal communication, A. Venditty, R. P. Scherer Corp., Detroit, Mich.

ary pressures of 7,000 p. s. i. and 3,000 p. s. i., the solution is deposited in several layers around the initial channel rather than in a pool as a needle would do, thereby creating a larger surface for greater dispersion of the solution.

The solution contained in the Metapule is hermetically sealed in an aluminum container under aseptic conditions (fig. 4). The Metapule has in its conical end a minute orifice through which the jet of liquid is expressed (fig. 5).

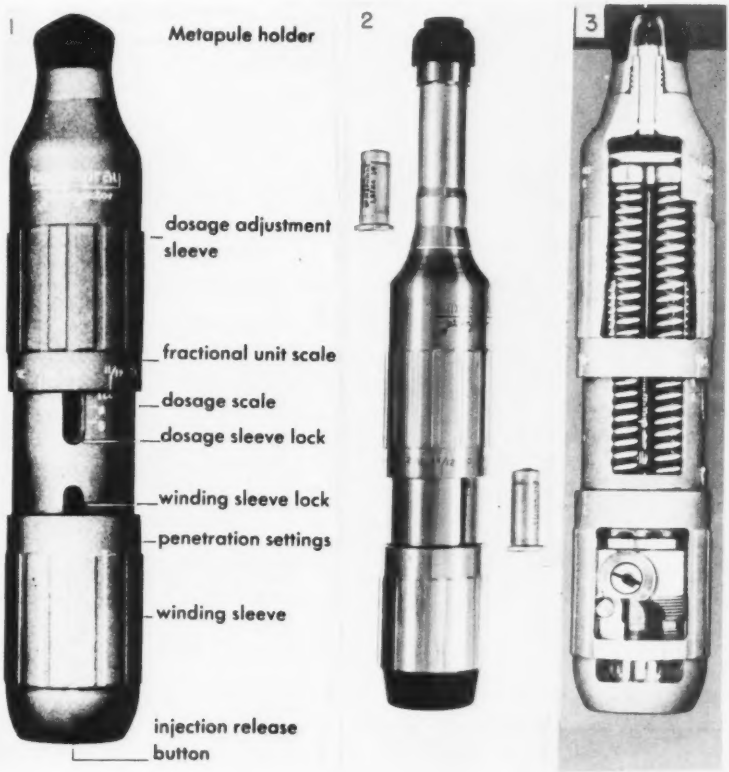

Figure 1. Jet injector for subcutaneous and intramuscular injection of medications and biologicals. Figure 2. Jet injector modified for dental use. Figure 3. Cross section of jet injector showing plunger (top), springs (middle), screw and nut (bottom).

The injector is made ready for injecting by pressurizing the springs through the turning of a winding sleeve (fig. 1). The Metapule is removed from its hermetically sealed container and placed into the front end of the injector. A cap is screwed on the end of the injector to hold the Metapule in place. The correct

dosage is selected by use of the rotating dosage scale and the injector is then ready for use.

As it is not necessary to touch the sterile Metapule during its removal from the container and placement into the injector it is only necessary to observe the usual technic of preparing the site for injection, as is done when using a needle and syringe.

Figure 4. Aluminum cartridge containing sterile Metapule of Xylocaine.

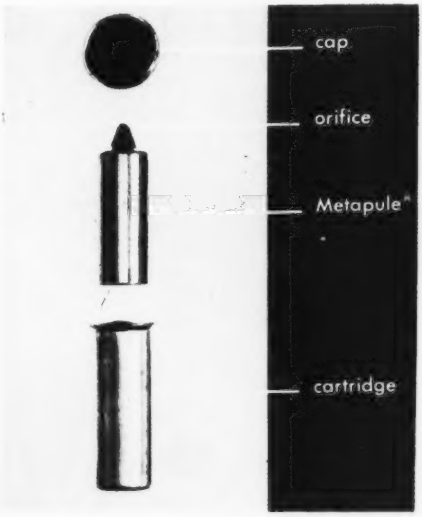

Figure 5. Exploded Metapule showing component parts.

Because the only injections into mucous membrane previously reported had been in the anal region,[3] it was decided to make test injections into the peritoneal and oral tissues of rabbits

to determine the resistance or nonresistance of those tissues to laceration. It was shown that the tissues were resistant to laceration. To determine the depth of penetration by the column of liquid, methylene blue was added to 0.1 normal saline solution and the series of injections repeated. The animals were killed and examined immediately following the injection and it was found that the depth of penetration was several millimeters. This was considered sufficiently deep to justify the expectation of successful anesthesia in dental use in man.

In all, 66 patients ranging in age from 10 to 37 years were used for this study. Usually only one injection was made per appointment but a number of patients had as many as four injections. The types of injections successfully administered were infiltration, conduction, and block anesthesia. Maxillary second and third molars were anesthetized by conduction anesthesia; maxillary centrals through the first molar, by infiltration anesthesia; and mandibular teeth, by use of the intraoral mandibular block and the mental foramen injection as well as the long buccal injection. The operative procedures successfully accomplished were the removal of caries and cavity preparations of all classes in both anterior and posterior teeth in both arches. The surgical procedures successfully completed were the extraction of anterior and posterior teeth in both arches.

The technic of making the injection did not differ greatly from the established technics using a needle. The same "puncture sites" were used, care being taken that the column of liquid entered at right angles to the area being injected. Any angle less than 90° resulted in a tendency for the column of liquid to make a small clean incision. There was difficulty in administering some of the injections due to the mechanical problem of properly placing the injector tip in the limited space of the oral cavity. The orifice sizes used in this study varied from 0.005 to 0.008 inch. The amount of solution used was 0.6 ml per injection, although successful injections were made using 0.3 ml. The anesthetic used was 2 per cent Xylocaine with epinephrine 1:100,000 and 1:50,000. The instrument was disinfected by removing the tip, washing it with soap and hot water, then placing it in benzalkonium chloride.

RESULTS AND DISCUSSION

The most striking finding was that the 66 patients denied any feeling of pain during the injection (fig. 6). This observation agrees with the findings of other investigators that pain was almost totally absent during injection.[1,5] Extraction of teeth, both mandibular and maxillary, and cavity preparation of all classes were successfully accomplished in 87 per cent of the cases (fig. 6). Unsuccessful attempts due to poor anesthesia were recorded in 13 per cent. In this latter group, additional

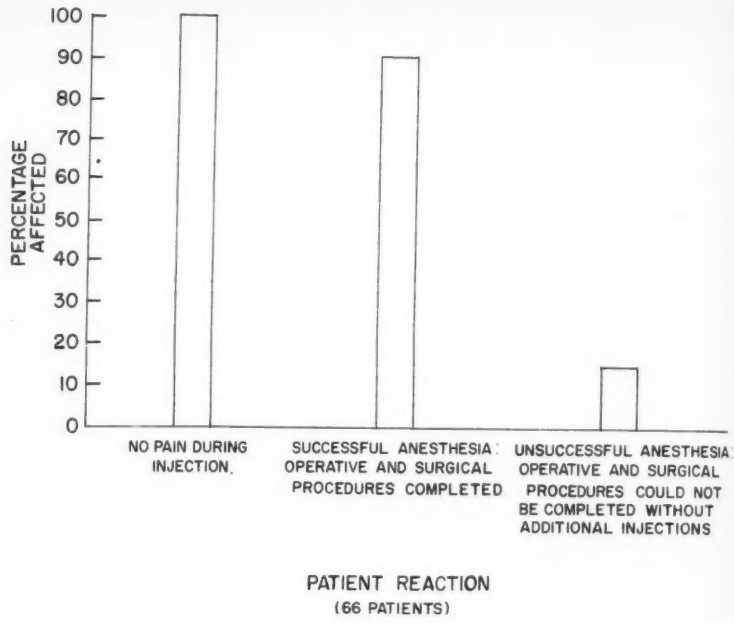

Figure 6.

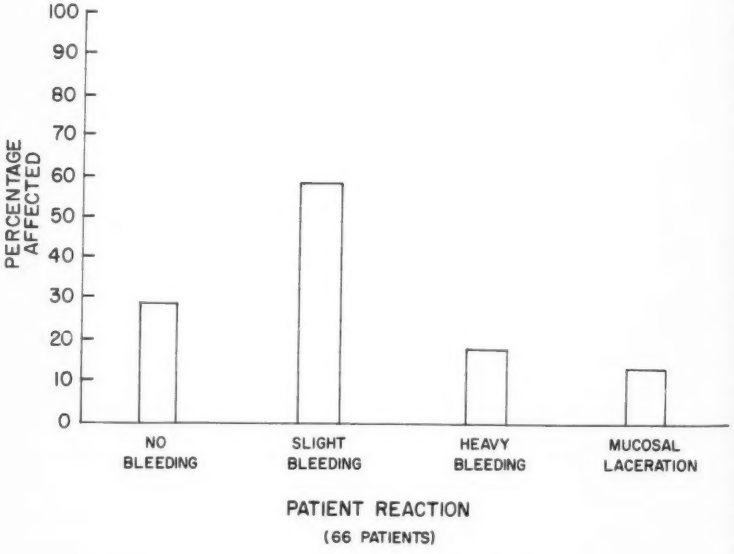

Figure 7.

injections had to be made to permit successful completion of the procedure. It should be pointed out, however, that reinjection of patients is required occasionally when using the customary needle and syringe. In 28 per cent no bleeding resulted following injection and in 59 per cent only slight bleeding was apparent (fig. 7). In 13 per cent, however, moderate to heavy bleeding was observed but was controlled easily by holding a 2- by 2-inch sterile gauze pad with pressure over the puncture site for one to two minutes. It was noted that mucosal lacerations were present in the majority of patients in whom bleeding was a problem. The incidence of moderate to heavy bleeding using a needle is negligible.

It was observed further that, in general, the larger the orifice, the greater was the tendency for laceration and bleeding. Further studies are needed to confirm this observation. Tenderness at the site of injection, persisting for 24 to 48 hours, was noticed in only a few instances. This occurs occasionally when using the needle and syringe technic. Healing following extractions was uneventful and examination of injection sites for periods extending up to 8 months revealed no abnormalities.

Inasmuch as there is theoretically no penetration of the mucosa by anything other than a sterile column of liquid, the hazard of transmitting infectious hepatitis probably is slight, although further data are required before it may be dismissed. It is further obvious that the danger of needle breakage during injection does not exist.

One might question whether the injection of 0.6 ml of liquid in a fraction of a second would result in a "ballooning" of the area injected. This has not been observed. Figge and Barnett[7] have shown, according to Pascal's law, that a small force amounting only to a few grams, is transmitted to the tissue in contact with the orifice. Preston, Goldman, and Thompson[8] reported that a mild degree of tissue distortion occurs in the immediate path of the fluid, but that there was no tissue destruction adjacent to this area. They further reported that repeated efforts were made, in dermatopathologic conferences, to determine whether the particular skin biopsy specimen under study had been infiltrated by a needle or a jet injector. They found it impossible to differentiate between the two technics without examining the immediate area. Biopsies done on very fragile lesions showed no distortion of architecture following jet injection into the tissues.

Warren and co-workers reported that in a large series of injections of saline-suspended biologicals no apparent trauma was caused. They further stated, "It appears reasonable to state at this time that, while considerably more study of jet injection is needed, the procedure will rarely cause undue trauma, pro-

vided certain basic precautions are observed."[9] Among these are the use of jets of a diameter of less than 0.008 inch and the proper selection of site and injected material.

SUMMARY AND CONCLUSION

It has been shown that dental local anesthesia of sufficient depth and duration to complete successfully routine operative and surgical procedures is feasible utilizing the jet injection principle.

Figure 8. Jet injector with dental tip in place.

Figure 9. Jet injector with dental tip removed.

Jet injection has the following advantages: (1) no discernible injection pain; (2) danger of transmitting infectious hepatitis may be less than with the conventional syringe and needle; (3) eliminates hazard of needle fracture during injection; (4) ease of sterilization; (5) the psychic trauma of needle injections is obviated.

Figure 10.

Disadvantages of jet injection are the high incidence of bleeding at the injection site and the cost of the jet injector and the Metapules.

These preliminary studies present the first basic change in injection technic in the history of dentistry. The results of this study warrant further investigation to determine the optimal orifice size and spring pressure for a jet injector designed

specifically for use in dentistry. An injector with which these factors could be determined has been designed and is shown in figures 8, 9, and 10.

ACKNOWLEDGMENT: The authors wish to thank Robert P. Scherer and Anthony Venditty for their technical advice.

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AMPUTATION STUMP PAIN

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THE most common complaint of the amputee seeking medical care is stump pain. A review of the Medical histories of over 7,000 amputees treated at this amputation center hospital during the past 12 years revealed that all amputees at one time or another suffer some pain. Not all patients, however, have persistent amputation stump pain.

In a Prosthetic Devices Research Project study at the University of California,[1] it was found that 80 per cent of all amputees were substantially free of pain. Approximately half of the remaining group, that is 10 per cent, experienced incapacitating pain which precluded successful rehabilitation. Experience with a larger number of amputees at this amputation center indicates that 94 per cent of the amputees can be successfully rehabilitated.[2] This implies not only freedom from persistent pain but also ability to carry on with a useful occupation.

The magnitude of pain an individual experiences is related to his so-called threshold of pain and to his conception of what constitutes pain. This may vary from a sensation of pressure to one of burning or tingling, and is often described in terms such as "like a hot wire run through the foot," "like a blow from a hammer," or "like a toe being pinched with a pliers."

A discussion of the cause of painful amputation stumps may be divided into three general headings: (1) conditions prior to surgery, (2) immediate postoperative pain, and (3) late postoperative pain.

CONDITIONS PRIOR TO SURGERY

Congenital amputees, as a rule, have little or no pain. On the other hand, a patient who develops gangrene as a result of thromboangiitis obliterans may have severe pain that even massive doses of narcotics fail to relieve. Following amputation these patients seem to have more than the usual degree of immediate and late postoperative pain.

From the Navy Amputation Center, U. S. Naval Hospital, Oakland, Calif.

Not all gangrene is painful. Gangrene caused by arteriosclerosis may be moderately painful. Gangrene following frostbite usually is mildly painful. Those patients who had major amputations as the result of frostbite, incurred in the Korean Conflict, suffered less. postoperative pain than those whose amputations were the result of severe trauma.

Neoplasm requiring amputation may or may not be painful. If the neoplasm becomes large, severe pain often ensues.

IMMEDIATE POSTOPERATIVE PAIN

Immediately following operation most amputees experience severe pain from surgical trauma. It is important to realize that postoperative pain following amputation is greater than that following the usual surgical procedures. The pain is more severe because amputation cuts across skin, subcutaneous tissue, fascia, muscle, periosteum, bone, blood vessels, and nerves. Postoperative edema is always present, causing pressure pain. Because the pain following amputation is generally severe, unusually large doses of narcotics are indicated for several days. It is rare to find a patient who does not require sedation following a major amputation. After a week or ten days post operative most patients require no sedation.

LATE POSTOPERATIVE PAIN

After a stump heals the majority of amputees may be subjected to stump pain at intervals for the remainder of their lives. Over 50 per cent of amputees experience stump pain or discomfort sufficient to discontinue temporarily the use of their prosthesis.

About 15 per cent of the amputees have major pain problems that are caused by (1) improper fit and/or alignment of the artificial limb, (2) dermatologic conditions of the stump, (3) bursitis in the amputation stump, (4) osteomyelitis in the stump, (5) trauma, (6) chronic anoxia of the terminal end of the stump, (7) osteoma and/or spurs, (8) neuromata, or (9) phantom limb.

Improper Fit and/or Alignment of the Artificial Limb

The time required for a new stump to adjust to an artificial limb is a difficult period. The initial fitting which amputees undergo is often a period of severe discomfort and, in some cases, actually painful. Because of the necessity for weight bearing on the stump, this is more marked in a lower extremity amputee. The skin, muscles, and bony prominences, especially over the weight-bearing points of the stump, require hardening and toughening so the amputee can wear the prosthesis without discomfort. The toughening process is exemplified by the irritation of the ischial tuberosity when breaking in an ischial weight-bearing, above-knee prosthesis.

There is a common saying among amputees that "the first three years are the hardest." On the average, amputees require a new artificial limb every five years. Most amputees require prosthetic services (alterations and repairs) several times a year. After amputees have become adjusted to their artificial limbs they generally can wear a prosthesis 15 hours a day. Every time an amputee is fitted with a new socket he may again go through this breaking-in period. This may be shortened substantially or even entirely eliminated by perfection of fit and alignment of the artificial limb. If the limb is poorly fitted and aligned, the breaking-in period is prolonged. If the limb is not in proper alignment, the amputee bears excessive weight on certain parts of the socket, resulting in irritation, discomfort, and pain in the stump. Alignment of the limb must be individually correct for each amputee.

When an amputee begins to use his artificial limb, the muscles which have been atrophied from disuse, and have formed new insertions, also undergo changes that often are painful. It is not uncommon for amputees to develop muscle spasms with cramping pain when they begin to use their artificial limbs.

Dermatologic Conditions of the Stump

The skin of an amputated stump is subject to disease and conditions that are peculiar to skin as a whole.[3] The skin and the subcutaneous tissues of the stump have not been designed to bear weight and consequently are more vulnerable to the stress and trauma of weight bearing. A factor affecting the vulnerability of the skin to various diseases is that the stump is snugly encased in its socket. Because of misfit of a socket, blisters, ulcerations, and painful calluses are not uncommon on stumps. Furunculosis is not uncommon in a region of pressure on the stump, and a furuncle on the stump is just as painful as one on the neck.

Dermatitis venenata caused by sensitivity of the skin to the material or finish of a socket may occur. Other dermatatides such as psoriasis, lichen planus, pityriasis rosea, or epidermophytosis generally are more violent on the skin of the stump.

As a prophylactic measure amputees are advised to keep their stumps and stump socks meticulously clean. Cleansing the skin daily with a soap containing hexachlorophene decreases the incidence of furunculosis.

Bursitis in the Amputation Stump

Bursitis may develop over a bony prominence if the protuberance is subjected to undue pressure by the socket. Bursitis over the head of the fibula is a frequent and troublesome occurrence in the below-knee amputee. Use of the Navy soft socket aids in preventing this condition.

463616 O—58——2

A painful bursa may develop over the terminal end of a Callander type above-knee stump. A bursitis of this type usually can be avoided by complete excision of the bursa about the knee at the time of the amputation. Once bursitis becomes firmly established in a stump, surgical excision is the treatment of choice.

Osteomyelitis in the Stump

Chronic osteomyelitis may be a source of continued pain in the amputation stump. The pain may be a sequel to postoperative infections following the initial amputation or it may be caused by pre-existing osteomyelitis in the bone. The principles of treatment in osteomyelitis are the same as those employed in the treatment of bone infection. Systemic chemotherapy alone is usually inadequate, but surgery and even re-amputation may be necessary. The severity of the infection, the extent of bone involvement, and the resistance to antibiotics indicate the treatment. In general the open-flap type of amputation is the safest procedure when osteomyelitis is present.

Trauma

Contusions or bone fracture in the stump may result when an amputee falls. An undisplaced fracture may be treated by application of a compression bandage and rest until resolution has occurred. Displaced fractures require reduction, fixation, and immobilization as indicated.

Anoxia of the Terminal End of the Stump

The end of the healed amputation stump is an area where tissue is left with an impaired blood supply.[4] When a portion of the vascular tree is amputated, the smaller remaining blood vessels dilate and carry out the function of supplying blood to the distal tissues. When disease of the vascular tree is present, the terminal tissues have even poorer circulation and the stump readily ulcerates.

For many years amputees have been fitted with open-end stump sockets. The weight-bearing points are the lateral walls of the socket, the flare of the bony prominences, and heavy tendinous structures. A piston action occurs between the stump and the socket during the walking cycle. There follows slight congestion and edema of the soft tissue on the end of the stump. This swelling is restricted by the lateral wall of the socket so that the only place the stump can swell is at the opening in the bottom of the socket. Chronic passive congestion of the stump end occurs and anoxia of the terminal tissues ensues. Over a long period of time the stump becomes irritated at the distal end, leading to stasis eczema (fig. 1) and, at times, ulceration. The histiologic changes occurring in the skin of the stump have been

described.[5] It is not uncommon to find chronic stasis eczema in the end of the stump and occasionally an acute dermatitis may complicate the stasis eczema. Not only does pain result, but the patient cannot use his artificial limb. Some limb fitters have found that by utilizing a piece of sponge rubber in the end of the socket to act as counterpressure, the chronic eczema can be controlled.

Figure 1. Terminal end of a below-knee stump showing chronic stasis eczema.

Presently at this center, all stumps are fitted with a closed-end socket. The socket has a sponge-rubber lining which is covered with flexible plastic sheeting (fig. 2). We have found that in most patients fitted with the closed-end socket, the distal end of the stump maintains a superior state of nutrition and that stasis eczema and edema promptly subside. The closed-end socket has an accurately fitted wall exerting counterpressure on the entire stump. In this way, chronic passive congestion and resulting anoxia are relieved. The closed-end socket is not a true end-bearing socket but is more accurately described as a

total-bearing socket, meaning that every part of the stump bears its equal share of the weight.

The suction socket with an air space at the bottom of the socket also is helpful in preventing chronic passive congestion of the terminal end of the stump.[6] The skin on the end of the stump is in contact with an air space which has a positive pres-

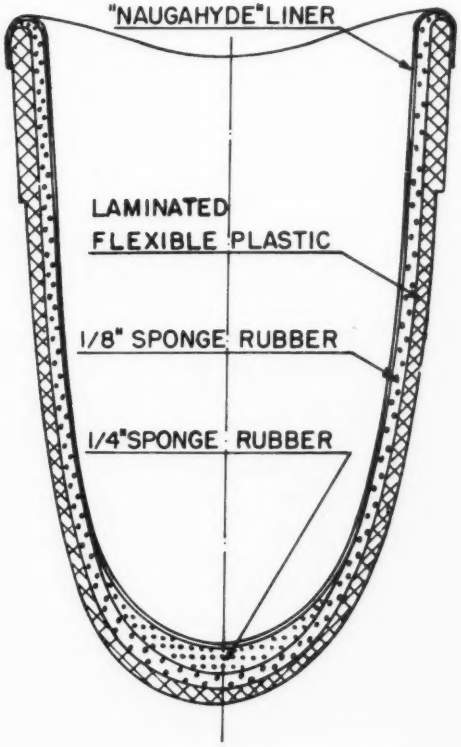

Figure 2. Details of the construction of the closed-end soft socket, sagittal section.

sure of one-half pound per square inch. When the amputee lifts his artificial leg during the swing phase of walking, the air then changes to a negative pressure of one and one-half pounds per square inch. This provides an alternating positive and negative pressure and is in effect a miniature "pavex boot." Over 80 per cent of the above-knee amputees can successfully wear the suction socket. Unfortunately, the suction socket is not without danger because of the critical values of fit and pressure. If the correct fit and pressure are not maintained, the suction socket

will cause edema, chronic congestion, anoxia, and ulceration of the stump.

Currently at this center an above-knee, closed-end, soft socket is used which utilizes the suction principle but without a free air space at the bottom of the socket. This new total-bearing socket prevents piston action between the socket and the stump and actually locks the stump in contact with the entire inner surface of the socket. The amputee releases the valve to permit removal of the stump from the socket.

Osteoma and/or Spurs

New bone formation at the amputated ends of bones is not an uncommon finding three to six months after amputation (fig. 3). The cause of new bone formation is obscure. It is apparent that some individuals have the tendency to form new bone more readily

Figure 3. Osteoma at the terminal end of an above-knee amputation three months postoperatively.

than others. Surgical procedures may have some influence on the incidence of osteoma and/or spurs. Ragged edges of periosteum and bone dust resulting during surgery are to be avoided. The surgical procedure employed at this center is to make a sharp incision through the periosteum and then strip the periosteum distally with an osteotome. The bone is sectioned just below the incision through the periosteum. The tissues are then gently lavaged with normal saline solution in order to remove the bone dust.

A bone spur may form if a fragment of periosteum remains in the soft tissue. A spur may be painless but is often extremely painful. It is not uncommon to see a long, thin bone spur growing from the end of the sectioned fibula (fig. 4). Osteoma may result from an attempt to use a bone graft on the end of the amputated bone. Some surgeons have attempted to place a bone plug in the terminal end of the bone in order to prepare a stump for end-bearing. Bone plugs are not necessary. The opened medullary canal of the sectioned bone will heal by forming a smooth, rounded table of compact bone in a matter of months postoperatively. An attempt to obtain a bone plug from the shaft of the amputated bone reduces the bone length and naturally produces a shorter stump. It is believed that length should be preserved. A long stump has far greater lever action and longer muscles which permit the prosthesis to be used more satisfactorily. If the bone plug should fail to unite and undergo aseptic necrosis, reamputation results in a shorter stump.

Another cause of bone spur is reattachment of the sectioned muscle to the raw surface of the newly sectioned bone. After amputation the muscle attempts to form a new insertion site. With the constant pull of the muscle on the periosteum where the muscle is attempting to form a new insertion, new bone formation occurs and a spur results. In order to prevent this type of spur formation, the sectioned ends of the muscles are sutured to their antagonists with mattress sutures of chromic catgut. The major muscle groups are sutured to each other, *i. e.*, flexors to extensors. In this way the muscles form their insertions on each other and in the scar tissue of the terminal end of the stump. In addition, by providing anchorage for the sectioned muscles, a stronger and more powerful stump results.

Conservative treatment of painful bone spurs and osteoma consists in providing relief in the socket. If relief cannot be provided, then surgical excision or reamputation is necessary.

Neuromata

Neuromata are the most common cause of stump pain, but they may cause little or no trouble. All peripheral nerves, upon amputation, heal by the formation of a neuroma at the distal end. If

the neuroma is adherent to raw bone, to the muscle, or to the surgical scar of the skin, it frequently becomes painful. Motion of the stump moves the skin, muscle, and bone. Each time the

Figure 4. Spur arising from the distal end of the fibula in a below-knee amputation.

stump moves, the attached neuroma is stimulated and pain results. This leads to pain in the stump and is often directly associated with phantom pain.

Stone[7] has emphasized that phantom pain is due to the irritation of the nerves, and the proper treatment of the nerves at amputation is of prime importance. The procedure of ligating the sectioned nerve ends or injecting them with alcohol at the time of amputation should be condemned. Clinical experience at this center indicates that at the time of amputation the nerve should be forcibly withdrawn distally from its sheath, cleanly amputated at the highest level, and allowed to retract upward into its sheath. The nerve sheath acts as a protection to the neuroma which develops later. In this way the neuroma cannot attach to scar tissue, which in turn is attached to some other tissue in the stump. The neuroma will be well protected high in the stump by the soft tissues and will be within the nerve sheath, its natural environment.

Should a painful neuroma be found in a stump, the mere excision provides only temporary relief because the new neuroma formed again attaches to scar tissue and the process reoccurs. The resection of the nerve trunk at a higher level likewise provides only temporary relief because a new neuroma forms on the proximal end of the nerve and adheres to the scar and the pain recurs. Some surgeons have reported excising a painful neuroma and implanting the nerve ends into a hole drilled in the bone.[8] This procedure may give temporary relief inasmuch as the portion of the nerve that is buried in the bone atrophies. A neuroma may form at the entrance of the bone where it is sutured to the soft tissues and pain may recur.

Examination of a stump for neuromata should be done with the stump relaxed. On palpating the neuroma the patient will describe sensations along the peripheral distribution of that nerve. It is possible to define the nerve involved from the patient's description of the distribution of pain in the part that has been amputated. Infiltrating the neuroma with procaine hydrochloride may give temporary relief. The treatment of choice is to excise the neuroma, pull down the nerve in its sheath, amputate it at a high level, and permit the nerve to retract in its sheath.

Phantom Limb

Much discussion has appeared in the medical literature regarding phantom pain. In fact, 112 references to phantom limb pain in amputated extremities were found in the literature covering only the past 10 years. Pain itself anywhere in the body is a peculiar type of phenomenon. Although the neuroanatomic pathways of pain have been established, the exact nature of pain, and in particular that of phantom pain, remains obscure. The University of California's report is an excellent treatise on phantom pain and sensation.[1,9]

Experience at this center is that all amputees have phantom sensation following amputation. The only exception to this rule has been in those with congenital amputations. It is interesting to note that children before the age of six or seven do not have phantom pain following amputation. After this age, they may develop phantom pain. Because of this phenomenon in children it has been deduced that the body image of self or the "corporal schema" is not developed until age six or seven years.[10]

The usual experience of an amputee is that he has phantom sensation which may be very vivid several weeks after amputation. These sensations gradually fade over a period of one to two years. Most amputees can recall their phantom limb at will for the rest of their lives. Some patients may go for periods of 10 to 15 years and then have a bout of phantom sensation and pain which may last for days or weeks. This latter type of phantom pain is generally from an irritation in the stump. The local irritation can be caused by the reasons previously described. If the cause of irritation is of a permanent nature, little or no relief occurs until the correct treatment is applied. If it is of temporary nature, the phantoms will generally disappear.

Fortunately phantom pain of a major degree exists only in about 2 per cent of amputees treated at this center. Another 10 per cent have temporary bouts of phantom pain which appear for a short period. The patient with constant severe phantom pain has one of the most difficult entities to cure. Reamputation of the stump is generally unsuccessful. Sectioning the nerve above the amputation site generally gives no permanent relief. Chordotomy, sympathectomy, excision of the post-central cerebral cortex, and even prefrontal lobotomy have a high percentage of failure.[11-14] Many of the amputees who have severe chronic phantom pain become either alcoholics or drug addicts. Very few of these patients are able to wear a prosthesis.

It is believed that phantom sensations and phantom pain are due to an abnormal excitation of the pain pathways involved. The pain pathway is so conditioned that the patient experiences almost constant phantom pain over the terminal distribution of the nerve involved. A strong habit pattern is thus developed. Phantom sensation and pain are often bizarre and phantoms are often misshaped and misplaced along the part of the missing extremity. Patients describe them as having a sensation of the leg being there, or "like a cold rope being drawn between the toes and foot being constricted in a wringer," or "shooting pains in toes, heel, and calf (foot normal length)." It is true that a patient who has severe permanent phantom pain generally develops a psychologic overlay, causing additional complications of his condition.

It is believed that the treatment of severe phantom pain or disturbing phantom sensations should be directed toward the cause of irritation of the stump locally.[15,16] Clinical research of this problem lends credence to the idea that peripheal abnormalities located in the stump play a part in the production of the phantom image and pain.[9]

The most common local source of trouble is the painful neuroma. Less common is the ill-fitting prosthesis and anoxia of the stump which in turn causes chronic irritation. If the cause is found and the proper relief provided, patients with severe phantoms still may experience their phantom pain for a considerable period afterward. The longer the patient has had phantom pain, the longer the recovery period will be after the cause has been removed. Due to the firmly established habit pattern, even after the cause of the abnormal bombardment of stimuli to the nerve is removed, the mechanism for phantom pain through the nerve pathways remains. The only hope for a patient with severe phantom pain is to remove the causative factor and anticipate that with time the conditioned habit pattern of the pain will gradually fade.

Attempts to incite irritations along the nerve segment may change the character of the phantom sensation but generally do not provide permanent relief. Russell and Spalding[17] found that if patients percuss their stumps with a small mallet, a temporary relief of phantom pain may be effected. It is believed that the percussion of the stump stimulates a new pathway for pain which becomes greater than the pathway already present. Ultrasonic radiation therapy has not given permanent relief of phantom pain; some patients have obtained temporary relief by this method.[18]

The treatment of a patient with pain admitted to this center is to carefully evaluate and remove the cause of irritation in the stump.

SUMMARY

Pain in amputation stumps result from a variety of local causes affecting the stump, and each patient must be evaluated individually. Phantom pain and sensation are caused by local irritation in the amputation stump. The proper treatment of amputation stump pain is to remove the cause of irritation in the stump.

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POSSIBILITIES AND LIMITATIONS IN THE USE OF CONVENTIONAL MEDICAL X-RAY FILM UNDER CONDITIONS OF NUCLEAR WARFARE

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THE sensitivity of all photographic film materials to nuclear radiation introduces some doubt as to their usefulness in areas of high nuclear radiation levels resulting from a nuclear explosion. Because of the complexity of all the circumstances involved it is difficult to make exact predictions on the limitations and protective measures to be taken. However, available data based on practical experience in nuclear explosions can be utilized to attempt an analysis of prevailing factors and to estimate whether or not conventional medical radiography will retain its place in emergency areas.

Medical x-ray film, of course, is radiation sensitive. But distinction must be made regarding its sensitivity when stored, as compared to that at the moment it is loaded in a cassette containing two fluorescent ("intensifying") screens. The screens are used to transform x-ray energy into light energy to which the film is much more sensitive. As a result, the film-screen combination is approximately 50 times as sensitive to diagnostic x-rays as the film alone. Further, the sensitivity of x-ray film alone (*i. e.*, without intensifying screen) to nuclear gamma radiation is only 1/20th its sensitivity to diagnostic x-rays. In other words, medical x-ray film, in effect, is highly sensitized only after it is placed in contact with the screens inside the cassette —*i. e.*, when stored in the manufacturer's box, the film sensitivity to nuclear gamma radiation is approximately 1/1000th of its value when actually used (with intensifying screen) by the radiologist. This means that medical x-ray film can be stored up to three days without significant damage and without additional protection at a radiation level equal to the maximum permissible dosage established to safeguard the health of occupationally exposed adults which is 0.3 roentgen per week. This maximum permissible dosage is, in general, the guiding figure for all protective measures. It is possible, however, that this

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dosage level can be exceeded temporarily, as in a nuclear blast or during transport through heavily contaminated areas. For this reason, it is desirable to analyze the conditions under which medical x-ray film might be stored and still be usable in nuclear warfare.

The following considerations are based on a tolerable fog level of 0.3 density units. The maximum dosage fulfilling this condition is approximately 0.1 roentgen for gamma radiation having an energy of 0.4 Mev or higher. Two basic cases must be distinguished: (1) an air burst of a nuclear bomb, and (2) a surface or subsurface burst of a nuclear bomb. In both cases the relative contributions and significance of the initial blast and of the time-delayed radioactive fallout to the total dosage exposing the x-ray film must be considered.

AIR BURST

There are three main sources of significant nuclear radiation after an air burst of a nuclear bomb: (1) The initial burst emits high energy gamma radiation and neutrons; (2) the neutrons of the initial burst induce gamma radiation on the earth to a considerable extent within a one to two mile radius from ground zero; and (3) radioactive particles are formed in the column and the fireball of the burst and yield the so-called "fallout."

The relative and actual importance of these radiation sources depends largely upon the location of the burst with regard to the surface, on the energy yield of the explosion, and the meteorologic conditions. The following considerations are restricted to a 1-megaton (equivalent TNT) explosion and to slant distances greater than 1 mile from ground zero. This latter restriction is justified because for closer distances the destruction by blast and fire, except for strong underground structures, would be virtually complete. The initial nuclear radiation probably would prove fatal to about 50 per cent of human beings even if sheltered by 24 inches of concrete. Thus, the possibility and need of diagnostic radiography would be eliminated for these reasons.

From data published by the Atomic Energy Commission[1] it can be derived that the initial total dosage (gamma radiation and neutrons) from a 1-megaton air burst at 1 mile slant distance will not affect significantly medical x-ray film if, at the time of the explosion, it is stored in such a way that it is protected by approximately 80 inches of concrete or 110 inches of earth in the direction of the blast. For a 20-megaton blast the required protection is provided by approximately 30 per cent thicker layers. In other words, storage in a basement corner on the floor will provide this protection except for an overhead burst. It might be worth mentioning that the attenuation of concrete and earth for neutrons is higher than for gamma radiation, and

because at distances greater than 1 mile the contribution of neutrons to the total dosage declines rapidly, sufficient protection against gamma radiation includes also protection against neutrons. For instance, the film material could be divided into two lots and stored in diametrically opposite corners of the basement in order to account for the unknown direction of the expected blast.

A small concrete vault providing some overhead shielding against scattered gamma radiation would provide additional protection. Basement storage proves increasingly safe for bursts at greater distances. If, for instance, the burst occurs at 2 miles slant distance instead of 1 mile, the total initial dosage will be only 1/1000th or, in other words, ordinary storage in the lower floors of concrete buildings would suffice.

As already mentioned, at distances greater than 1 mile the neutron-induced activity will be small and readily be attenuated by the protective measures described.

With regard to fallout from an air burst, the amount of contamination will be appreciable only in a limited area around ground zero, depending on the height of the burst, the energy yield, and the time elapsed since the explosion. At Hiroshima and Nagasaki, for example, the induced radioactivity on the surface was believed to be negligible. At Bikini, however, where the height of the burst was relatively low, the induced gamma radiation from radioactive sodium formed in the water reached two hours after the burst a level of 1 roentgen per hour. This dose rate would suffice to render medical x-ray film unusable within 15 minutes. Storage facilities, however, as mentioned before, would suffice for protecting film material, even in this case. But such a dose rate would demand evacuation of the area in any case in order to avoid long-period accumulation of damaging radiation doses. The local fallout soon after the explosion will be relatively unimportant for air bursts. Over longer periods, however, the fallout will extend over larger areas, but time for protective measures usually will be available.

SURFACE BURST

With a surface or subsurface burst the local fallout will assume major significance. Additionally, destruction near ground zero will be complete within a wide area, thus eliminating all means for medical radiography, whether based on the use of photographic material or other recording systems, *e. g.*, xerography.

In a surface burst, large amounts of debris, earth, and dust are taken up into the fireball where they are fused or vaporized and become intimately mixed with the fission products. The larger and heavier particles will descend from the column within about an hour and will form a roughly circular pattern around

ground zero. The smaller particles are carried upward and may spread out some distance before they begin to fall. The time taken to reach the earth and the horizontal distance traveled will depend on the height reached, the size, and the wind pattern. Very fine particles may remain suspended for long periods and may travel many thousand miles. Most of the larger particles, however, probably will reach the earth as local fallout within a few hundred miles.

Protection against fallout radiation presents difficult problems because of its widespread and persistent character. The contaminated area can be expected to extend well beyond that in which casualties result from blast, thermal radiation, and the initial nuclear radiation. Protective measures can be classified into passive and active categories. Passive protection implies remaining in the contaminated area and seeking shelter. Even basements of frame houses can attenuate considerable fallout radiation provided that commuting from and into outside areas is avoided. Active protection entails evacuation and/or decontamination. Both procedures inevitably are hazardous because they involve exposure of operating personnel.

Seeking shelter in relatively closed structures may be regarded as the best initial protective step. If commuting to outside areas is kept to a minimum, then the radiation level can be kept very low, and properly stored x-ray film material will hardly be affected. The decay of the fallout radiation with time will rapidly improve the situation, allowing also for improvised protective measures for all photosensitive materials. Continuous monitoring of the radiation level is essential. If film material, stored in the sheltered area at the time of the burst (*e. g.*, in a normal hospital) should become contaminated or exposed to the initial blast, its replacement by new material from an outside source through a contaminated fallout area becomes a problem. It must be transported in vehicles which offer some degree of protection, *e. g.*, by suitable shielding or distance. For instance, if the material is flown into the area by helicopter, both height above ground and reduced time of exposure can keep the radiation level below a damaging threshold even over heavily contaminated areas. Once in the shelter, the film material will be safe.

Two features of fallout radiation are characteristic: (1) its relatively slow build-up with time (slow in comparison to the initial burst radiation which is delivered within a few seconds after the blast) and (2) its subsequent decay. Depending on distance and meteorological conditions, evacuation or seeking shelter are the two alternative protective measures. During the build-up period a good deal of protective emergency measures in the shelter area can be arranged, particularly if personnel trained for emergency are available. The shelter, of course, must not

be abandoned until the time decay of fallout radiation ensures radiation safety.

A short remark may be added with regard to the contamination of water used for processing x-ray films. If the water contains radioactive particles, they might appear as black spots on the developed films, but only if the particles are present in the developer where the time of contact is restricted to 3 to 5 minutes. In cities where the water from a reservoir is subjected to regular treatment (coagulation, sedimentation, and filtration) much of the radioactive material will be removed. Underground sources of water generally will be free from contamination, as opposed to rain water, which is likely to be heavily contaminated. In cities where the water is taken directly from the river and merely chlorinated it may be unfit for consumption but still be usable for film developing. The provision of a small ion-exchange column or water distillation unit for emergency use might be considered. A home water softener would serve the same purpose. Water already in the sheltered area at the time of the explosion, *e. g.*, in water heaters, will be free of contamination. And even if small black spots due to contaminated processing solutions should be visible on the developed radiograph, this normally should not be detrimental to its diagnostic value. A repeat radiograph would be helpful in critical cases.

Summarizing, it can be said that conventional medical x-ray film still would have its place in areas affected by nuclear radiation. This fact is often overlooked. The use of film instead of other recording means remains preferable in view of the fact that the dosage required for a good radiograph is considerably lower for medical x-ray film than for any other system known so far, thus avoiding any excess radiation in addition to the level already existing.

For example, the dosage required to obtain a deep body radiograph by means of xeroradiography is approximately 5 to 6 times higher than by means of conventional radiography using x-ray film.

Consequently, the protective measures for storing and handling film are well worth the efforts.

SUMMARY AND CONCLUSIONS

The sensitivity of medical x-ray film in its original container to nuclear radiation is approximately 1/1000th of the sensitivity which the film assumes when exposed to diagnostic x-rays while in contact with intensifying screens.

Near ground zero of a nuclear explosion medical x-ray film and equipment are rendered useless. However, general destruction in this area is so complete that no means for medical radiography would be available, regardless what radiographic system would be used.

For distances greater than 1 mile from a nuclear air burst, storage in a basement would provide sufficient protection for medical x-ray film from the initial blast.

For surface blasts, protection against fallout radiation must be considered in addition to shielding against the initial blast. Basement storage of film material will be adequate in most cases. For transport of film through heavily contaminated areas, monitoring of the dosage to which human life is exposed will indicate the time limit up to which film might be usable.

As an additional precaution, particularly against scattered gamma radiation from the initial blast, two small concrete or brick vaults to be placed in opposite basement corners are recommended for film storage.

The danger of reducing the diagnostic value of a radiograph due to contamination of the developer solution is considered insignificant.

Medical radiography using conventional x-ray film will be feasible in the neighborhood of a nuclear explosion without extreme measures for protecting the film.

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A NONSMOKER SPEAKS OF SMOKING

"Physicians who smoke cannot in honesty recommend no smoking to their adult patients. Not, that is, unless they preface the warning with that trite phrase, 'Do as I say; not as I do.' The best argument against a physician smoking is that for the most part and for the longest time the odor from his mouth carries the memory of a cuspidor in a saloon. Needless to mention, the writer of these sentences is a nonsmoker from way back, not a Johnny come lately to the abstainer's bench. Don't smoke if you tell your patients not to."

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MEDICAL ECHOES

WALTER L. BIERRING, *M. D.*

IT is difficult to select a theme worthy of this occasion, yet it may be of interest to recall certain impressions gained during the formative period of a medical life, of personalities and epochal events that sound an echo down through the years, and thus endeavor to estimate their part on the medicine of this later day.

Viewed through the perspective of memory, three outstanding personalities—Billroth, Pasteur, and Osler—left an enduring impress and may form the basis of the thoughts I wish to present.

I came into medicine in March 1892, some 65 years ago, after the completion of a graded course of six months each with a teaching hospital of 50 beds. Yet in this somewhat limited teaching environment were two inspiring spirits that opened up entirely new fields of thought for the inquiring student. One was the professor of anatomy, later a leading surgeon, who had received a medical degree from two universities in this country, a member of the Royal College of Surgeons of England, with graduate studies during four years in the laboratories and clinics of London, Berlin, Vienna and Paris, including a course in bacteriology at the Royal Institute for Infectious Diseases in Berlin with Professor Robert Koch. He brought the first oil immersion lens, centrifuge, and stomach tube to the Iowa University Medical School, besides presenting an unusual course in neuroanatomy and demonstrations in neuropathology.

The other was the professor of chemistry who gave the first course in biochemistry at the institution, and had spent the last four summer vacation periods in the laboratory of Professor Hoppe-Seyler in Strausburg, then the leading physiological chemist in Europe.

Lecture presented at Walter Reed Army Medical Center, 25 November 1957. Dr. Bierring is Director of Gerontology, Heart and Chronic Diseases, Iowa State Department of Health, Des Moines, Iowa. He is a former president of the American Medical Association and of the National Board of Medical Examiners, and a former chairman of the American Board of Internal Medicine and of the American Board of Preventive Medicine.

These two leading scientists inspired the urge for further study—and perhaps you will share with me the thrill of being suddenly transported a few weeks following graduation into the field of opportunity such as was offered by medical Vienna during its so-called "Glanz-periode."

This famous university medical school with its laboratories in the basic sciences was grouped around the general hospital "Das Allgemeines Krankenhaus" with its 2,600 beds. Within its walls at that time there were over 10,000 births annually, and more than 2,700 deaths. Great names were then a part of Vienna medicine. There was Northnagel, Kraus, Neusser, and Kovacs in internal medicine; Billroth, von Eiselsberg, and Albert in surgery; Lorenz in orthopedic surgery; Chrobak, Schauta, and Braun in obstetrics and gynecology; Frankl-Hochwart and Krafft-Ebing in neurology and psychiatry; Kaposi in dermatology; Kolisko, Weichselbaum, Paltauf, and Gruber in pathology and bacteriology; von Ebner in histology; Obersteiner in neuropathology; Fuchs and Stellwag in ophthalmology; Politzer, Gruber, and Urbantschitsch in otology; and Schnitzler, Hajek, and Chiari in rhinolaryngology. Inasmuch as autopsies were the rule, unusual opportunities were offered for the study of gross and microscopic pathology.

It was an era of the therapeutic nihilism when the art of clinical diagnosis reigned supreme with the subsequent autopsy report to confirm or change the clinical conclusions. It was said of Professor Neusser in internal medicine that he sent 100 consective clinical diagnoses to the autopsy room without an error.

By a fortunate circumstance I early came to know Assistant Professor Anton von Eiselsberg, and through him came under the influence of his great chief, Professor Christian Albert Theodor Billroth, then recognized as the premiere European surgeon and pioneer in visceral surgery.

In 1892 Billroth was completing 25 years of professorship in the Royal University of Vienna, which occasion led to a wider publication of the various episodes of his eventful career. He was born in Bergen, on the island of Rügen, but received his general and medical education at the universities of Greifswald, Göttingen, and Berlin.

At 24 years of age, he became assistant to Professor Langenbeck of Berlin, where he had an excellent opportunity to learn operative surgery. However, his studies on comparative and pathologic histology of the spleen, the structure of lymph nodes, periostitis, resorption and normal growth of bone attracted so much attention that in 1858 he was offered the professorship of pathology at the University of Greifswald. This he declined,

but two years later he accepted the chair of surgery at the University of Zurich, Switzerland. It was here that he completed his monograph on "Cocco-bacterium septica" that presented a true concept of wound infection. While at the University of Zurich the first edition of his *Handbook of Surgical Pathology and Therapy* was published, which became so popular because of its pleasing and clear presentation of the various subjects, that it required a new edition almost every year. In the introductory chapter he stressed the necessity that "The Surgeon should combine general medical knowledge based on capable anatomical and physiological background, and a surgeon who is able to do that and has at his command the artistic side of surgery, may boast of having attained the highest goal in general medicine."

At the ceremony attending the silver anniversary of Billroth's professorship in Vienna, his colleague, Professor Albert, referred to the Faculty requirements for the professorship of surgery in the Vienna school, which included "the highest art as a practical surgeon and scientific investigator, as well as in physiologic and pathologic research; furthermore a teacher, operator, writer and a pleasing personality." All these were met by Billroth when he answered the call to Vienna, at which time he was 38 years of age.

This is all more significant when we consider the period 1867, nine decades ago. In his new field he reached his greatest prominence as a pathfinder, when he introduced surgical treatment in gastrointestinal disease. He was also the first to undertake total extirpation of the larynx and the esophagus, as well as gastroenterostomy and stomach resection, which opened for surgery a wide and productive field. He contributed to practically every field of surgery. I was privileged to be present at several plastic operations on the face by Billroth, which were done as carefully and expertly as a pyloric resection or extirpation of the larynx.

I also witnessed in 1892 my first thyroidectomy and removal of the Gasserian ganglion by von Eiselsberg, first assistant to Billroth. During that year this brilliant young surgeon reported his interesting researches on hypoparathyroidism in relation to tetany.

Billroth and his pupils Czerny, Gussenbauer, von Hacker, Wölfler, Gersuny, von Mikulicz-Radecki, von Eiselsberg, Salzer, and Fraenkel formed a school of surgery that became a nursery of professors, as all of the aforenamed became teachers of surgery in leading European universities. Billroth was a monumental figure, such as comes but once in a generation, from whose presence a light emanates that shines through the years ahead, reflected in part by the brilliant achievements of American surgeons in the early part of the twentieth century.

Billroth had a gracious manner, spoke a pure German, and was very kind and considerate to American students and physicians. Frequently at the close of a clinic session or ward visit, he would explain certain features of the operations performed and the diagnostic problems involved. His knowledge of physiology and pathology added distinctly to the discussion. Occasionally he would speak of a delightful musicale with his friend Johannes Brahms the evening before. This great composer dedicated to Billroth two of his string quartets. In his letters, *Briefe von Theodor Billroth,* published in 1895, one year after his death, we have a glimpse of his beautiful soul and sterling character, and gain a further realization of his intimate friendship with Brahms, Hanzlick, and other great figures in the field of music, as well as with the leading surgeons of his time.

It was in keeping with the sentimental Viennese to produce a photograph at the ceremony of the 25th anniversary of Billroth's professorship, in September of 1892, which portrays Billroth standing on the veranda of his summer home at St. Gilgen in the Austrian Alps, viewing the beautiful autumn foliage of the surrounding hills, and subscribing his signature with the words of Hebbel, "Dies ist ein Herbsttag wie ich keinen sah." (This is an autumn day the like of which I never saw.)

The last two decades of the nineteenth century was a period when bacteriology was becoming an integral part of medical and clinical investigation. Two schools of this new science were shaping the current of thought in all fields of medicine, that of Louis Pasteur in Paris and Robert Koch in Berlin.

The teachings of Robert Koch predominated in the German and Austrian schools. His discovery of the tubercle bacillus in 1882, the demonstration of the *Spirillum cholerae asiaticae* two years later, as well as the comprehensive studies on the anthrax bacillus had established his fame as a bacteriologist. His introduction of solid culture media had placed all bacteriologic investigations on a firmer foundation.

During the years 1892 and 1893 there had been opportunity for taking short courses in bacteriology with Professor Paul Ernst in Heidelberg and Professor Max von Gruber in Vienna, both former assistants of Professor Robert Koch. The course in Heidelberg was interesting. It was the first formal course attended in the new science. For the first time spores and cilia were successfully stained. The cultures of tubercle bacillus and spirillum of asiatic cholera used for study were from the original strain first developed by Koch, 10 and 8 years previously. The existing epidemic of cholera in nearby Hamburg added a further interest. For the first time the characteristic rice water intestinal contents were observed.

Pasteur was generally recognized as the father of bacteriology, the discoverer of a new world, that of the infinitely small. His studies in bacteria extended back to 1854, and early recognition that all fermentations were due to micro-organisms—the making of wine through fermentation of the grape, the souring of wine to produce vinegar, the decomposition of all animal matter by bacteria and the final overthrow of the theory of spontaneous generation.

His first studies in disease were with chicken cholera, and the demonstration of a small coccobacterium as the causative agent. He was able to produce a vaccine through attenuations of cultures grown at a lower temperature than is natural for fowls—which proved very effective as a protective agent.

His further epoch-making demonstration with protective vaccines in anthrax and blackleg saved the cattle industry in France. He was equally successful in controlling the diseases of silkworms, where he first recognized the difference in virulence in infective micro-organisms. This led rapidly to the study of wound infection.

In 1873 came the historic letter to Pasteur from Joseph Lister, the surgeon of Edinburgh, reporting his first successful results in the use of surgical antisepsis, based on the studies of Pasteur.

Less than twenty years later, in the fall of 1892, these two great leaders met on the stage of the Sorbonne, in Paris, at the exercises for the celebration of Pasteur's 70th birthday. Joseph Lister gave the principal address on this historic occasion.

During the eighties had come the remarkable studies in rabies, and the development of antirabic protective vaccination.

It was, therefore, one of life's privileges to come to the Pasteur Institute in Paris in the early spring of 1894, then No. 25 rue Dutot, now renamed "rue le docteur Roux," near the Boulevard Pasteur. It is interesting to recall that the laboratory table at the Institute assigned to me had just been vacated by Dr. Charles F. Martin of Montreal, later for many years Professor of Medicine and Dean of the Faculty of Medicine of McGill University.

The Pasteur Institute had been built in 1888 by funds collected by popular subscription as an expression of a grateful French people in recognition of Pasteur's scientific discoveries in saving the wine, silk, and domestic animal industries for France, as well as his epoch making contributions to medical science and the control of human diseases.

In 1889 Pasteur had transferred the Directorship of the Institute to his pupil and assistant of many years, Dr. Pierre Paul Emile Roux. The associate Directors were Doctors Metchnikoff, Borrel, Martin, Chamberland, and Calmette. The principal contacts

were with Roux, Metchnikoff, and Borrel, and it may be of interest to record a few impressions retained of each.

Dr. Roux had been so closely associated with Pasteur, particularly in his early work on anthrax and rabies, that he breathed the very spirit of the Master. He had been the principal assistant of Pasteur during the period of the preventive treatment of rabies. In 1887 he had demonstrated with Yersin the specific toxin of the bacillus of diphtheria and the bacillus of tetanus. Dr. Roux was of slender build, slightly stooped, always wore a black skullcap, had a kindly face, with a distinctly penetrating eye, and an inspiring personality. His was a life devoted to science. He had not married and had his living quarters in the Institute; there he also had his last sleep on November 3, 1933, at the age of 80 years. A simple marble tablet in the courtyard of the Institute marks his resting place.

Dr. Elie Metchnikoff, the Russian biologist, had been an associate of Pasteur for a number of years, and practically all of his further researches in phagacytosis and immunology were carried on in the Institute. A vivid memory remains of the interesting figure he presented as he walked across the courtyard to and from the animal quarters. I can still see the large head with black beard and long locks of hair, body bent slightly forward, with test tubes of culture media in one hand, and glass pipettes in the other, and from the side pockets of the long laboratory gown, a number of guinea pigs and white rats sticking out their heads. On one occasion I accompanied him to the animal quarters to obtain saliva from a dog with rabies. The dog was muzzled, but snapping his jaws viciously. Dr. Metchnikoff used one of the long pipettes prepared in the laboratory, inserted it into the mouth of the dog, and withdrew by sucking sufficient saliva for his purpose, which is an exhibition of rare scientific courage.

Dr. Metchnikoff could lecture with equal facility in French, English, and German, as well as in his native Russian language. He died in 1916, and his ashes are kept in an urn placed in the library of the Institute.

Dr. A. Borrel, a bacteriologist, was interested at the time in investigating the parasitic origin of cancer and other malignant tumors. The plates and illustrations of pseudoparasites and cell inclusions, accompanying his publications in 1894-1895, resemble much of what was published by later investigators. His conclusions as stated then are interesting: "It is possible that further research will determine that tumors are caused by sporozoa, bacteria or yeasts, and while all these hypothesis are permissible, but up to this time such do not appear to be demonstrable." After World War I, Dr. Borrel became professor of bacteriology at the University of Strasbourg.

The course in bacteriology at the Pasteur Institute covered a period of from 10 to 12 weeks, upon the completion of which the student was permitted to carry on independent studies and investigations. The forenoon was devoted to a lecture demonstration by Roux, Metchnikoff, or Borrel and the afternoon to practical exercises pertaining to the topic under consideration for that day. These included classification of bacteria and micro-organisms; preparation of culture media; glass blowing; study of microbes of the air, water, and soil, and pathogenic micro-organisms; culture and staining characteristics; inoculation of animals; virulence; vaccines; toxins and antitoxins. It was difficult to absorb all the new knowledge that was presented. The demonstration of filterable and nonfilterable forms of microbic life was demonstrated by the use of the porcelain filter, developed by Chamberland, Assistant Director of the Institute. It was the first suggestion that living viruses existed of filtra-microscopic size—later demonstrated with the advent of the electron microscope. Practical demonstration was made of the purification of public water supplies by filtration through sandy soil, including a visit to the sewers of Paris, and the sewage disposal and soil filtration purification plant at Gennevilliers, a suburb of Paris. The importance of denitrifying bacteria in the soil in connection with fertilization was recognized. The demonstration by Pasteur of fractional exposure of higher temperature prevented wine from souring and forming vinegar, thus the advent of pasteurization.

Opportunity was offered for the study of special forms of infective micro-organisms, such as the three types of *Bacillus tuberculosis*—avian, bovine, and human; bacillus of glanders; bacillus of leprosy; organisms causing hog cholera, Asiatic cholera, actinomycosis, Madura foot, and relapsing fever; malarial parasites; coccidiosis of rabbits; ringworm *(Trichophyton tonsurans);* favus *(Trichophyton schoenleini);* as well as the demonstration by Borrel of coccidia-like cell inclusions in cancer, vaccinia, and variola.

Special attention was given to the study of rabies or "le rage" in dogs and rabbits, the latter having the paralytic type of the disease when produced experimentally.

It was demonstrated that the rabies virus was contained in the spiral cord and other parts of the central nervous system in animals dying from rabies. An emulsion of sections of such spinal cords was used for inoculating animals such as the rabbit, and with each successive inoculation the virulence increased until the animal always died on the sixth day. This became the fixed virus, or "virus-fixe" of rabies.

Sections of spinal cords with this fixed virus were suspended in flasks, exposed to dehydration with copper sulfate, resulting in a gradual attenuation of the virus, until by the 21st day it had lost most of its virulence. The attenuated form of the rabies virus, or vaccine, formed the basis of protective vaccination in human persons, or dogs, bitten by rabid animals. These vaccinations were carried out in the dispensary of the Pasteur Institute. Similar institutes for this purpose were later established in different parts of the world.

In this year, 1894, under the direction of Dr. Roux, diphtheria antitoxin or antidiphtheritic serum was produced for the first time on a large scale, by the immunization of horses to the toxin of the diphtheria bacillus. The blood serum of such immunized horses was found to have sufficient antitoxic units to be of curative value in the treatment of diphtheria, as well as for the purpose of protective vaccination. The antitoxin units as determined, formed the basis of serum therapy in diphtheria, being a confirmation of the researches of von Behring and Kitasato in Germany of the properties of serum from animals rendered immune against diphtheria and tetanus.

Between February and July of 1894, 300 patients with diphtheria were treated in the nearby Children's Hospital with antidiphtheria serum as prepared in the Institute, resulting in a remarkable lowering of mortality rate from 51 per cent to around 25 per cent. For purpose of control and comparison, a similar number of patients with diphtheria at the L'Hôpital Trousseau were treated by the older methods of therapy, and the comparative results, in observing the patients from day to day as well as in in the mortality rate, were dramatic and left a vivid impression.

Two personal contacts with Pasteur remain vivid in memory. While Pasteur had his residence in the Institute, he was away a great deal, usually at his summer residence near Paris, so that his visits to the laboratory were real events. One of these visits, early in July 1894, was particularly so for the Institute, because on that day Doctor Yersin, a former assistant director, returned from China with organs and tissues showing the pathologic changes of bubonic pest or plague, and pure cultures of bacillus pestis, the specific causative micro-organism of this disease, demonstrated independently by Yersin in China and Kitasato in Japan, both being published in 1894.

The entire day was given over to this interesting demonstration. The Master (Pasteur) remained something over an hour, and freely expressed his gratification over the eventful exhibit, yet added with a sigh, "Mais, il y a encore beaucoup a faire." (But there is still much to do.) No doubt there was in the minds of some that day the memory of the Black Death of the 14th century, when

one third of the world's population died of the plague, and the great epidemic of bubonic pest in London in the 17th century.

Another eventful day brought the privilege of an extended audience with Pasteur. I accompanied Dr. Roux to the Master's rooms on the second floor of the Institute, where we found him seated in his chair with his left hand against the side of his face and wearing the round cap seen in a number of his portraits. He spoke in French with a slight hesitancy in speech, due to a partial facial paralysis following a cerebral vascular accident in 1868. He expressed a personal interest in my work of the Institute and inquired particularly regarding the progress of bacteriology and medical education in America. He was familiar with the work of Dr. Welch in Baltimore for whom he expressed his high regard. Pasteur was especially interested in the development of two of the newer universities, that of Leland Stanford in California and the University of Chicago, and marveled at the liberal donations made by Senator Stanford and Mr. John D. Rockefeller for the purpose of higher education. He added this comment, "Ici il faut toujours tirer le diable par la queue." (Here it is always necessary to pull the devil by the tail.)

He was assured that it took a certain amount of tail pulling in our country, although philanthropists were manifesting increasing interest in assisting educational institutions. He warded off any reference to his personal contributions to the science of bacteriology, but expressed his gratification that the Institute was able to offer opportunities for investigators from all parts of the world to continue their studies in the field of bacteriology and infectious diseases. Adieus and kind wishes ended a memorable conference that left an enduring memory.

The health of Pasteur continued to fail the following year and a final cerebral hemorrhage, on September 28, 1895, quenched forever one of the most brilliant minds ever bestowed on a member of the human race. Of him it may be said that he changed the medical thought of the world and brought forth a new era in medicine which extends down to this modern day. He rests in the Institute. His tomb is regarded as the finest example of Italian mosaic art in existence. At each subsequent visit to the Institute, the last four years ago, I have paid my silent tribute.

Many American medical leaders of that day had sought further training in European medical centers and coming back with the flavor of an older civilization brought the impact of the laboratory and clinical teaching at the bedside to the door of every institution concerned with the training of physicians.

In the forefront of such leading spirits was Dr. William Osler. It is difficult to present a true concept of the inspiring influence

of Osler on the medical student and young physician, as well as his part in the program of medicine of his period. He was a Canadian by birth, fortunate in his early teachers, and a graduate in medicine from McGill University in 1872 at 23 years of age. Instead of settling down in active practice, he followed the urge for further study with the leading physicians of Edinburgh, London, Berlin, Vienna, and Paris. In Berlin, Virchow was in his prime as the foremost pathologist; Langenbeck in surgery; Traube and Frerichs in medicine; and Du Bois-Raymond and Helmholtz in physiology and physics. In Vienna, Hebra led in dermatology and Politzer in otology. Osler attended a variety of courses with Braun in obstetrics, all at the Allgemeines Krankenhaus, his purpose being to study general medicine, as it represented British and European medicine of that day. In Paris he came in contact with Marie and Charcot, leading French neurologists.

Upon his return to Montreal in 1874, he practiced medicine for a few months and then was elected Lecturer in the principles of medicine at McGill University. After one year in this position, he was named professor of physiology, in 1876, and pathologist to the Montreal General Hospital, and in 1880 physician to this hospital.

In 1884, after 10 years of teaching at McGill, at 35 years of age, he closed his Canadian period to assume the Chair of Clinical Medicine at the University of Pennsylvania to succeed Dr. William Pepper who became Professor of Medicine. His teacher and faculty colleague, Dr. R. Palmer Howard, stated that McGill lost its "potent ferment" when Osler migrated to Philadelphia. The same year he was elected to the presidency of the Canadian Medical Association and the following year returned from Philadelphia to preside at the annual meeting held at Chatham in Western Ontario.

In 1885 he gave the Goulstonian Lectures on Endocarditis before the Royal College of Physicians in London.

Osler was warmly welcomed by the medical leaders of Philadelphia—Pepper, Tyson, Stille, Silas Weir Mitchell, Samuel David Gross, J. C. Wilson, Horatio C. Wood, Ashurst, and others, and soon became a part of medical Philadelphia.

It was a time when medical teaching consisted largely of formal lectures and amphitheater clinic demonstrations of unusual disease conditions. The institution of ward walks and teaching clinical medicine at the bedside was received with enthusiasm by students and, particularly, the younger members of the teaching staff.

The wards of old "Blockley" or Philadelphia General Hospital provided an abundance of interesting disease conditions. Instead

of devoting his afternoon, as was custom, toward developing a private practice, Osler spent the time at Blockley hospital to perform postmortems, the careful records of which are treasured traditions of this hospital.

His interest in the library of the College of Physicians of Philadelphia led to wider use of the same by students and physicians.

Then came the call to Baltimore in 1889 to become one of the "Big Four"—Welch, Halstead, Kelly, and Osler—to develop the school of medicine at Johns Hopkins University on a plane of high standards unique at that time. This new environment and association with leading spirits offered unusual opportunities for one of Osler's training and experience to advance medical teaching and practice, as well as the highest professional ideals.

Here in 1892 Osler was able to complete his first edition of his *Text Book of the Principles and Practice of Medicine,* which ushered in a new era in clinical medicine and formed a milestone in the progress of medical knowledge. During the succeeding three decades, nine revised editions appeared, and for those of us who were asked to teach both in pathology and clinical medicine, it formed a constant guide through the changing periods of medical practice.

Osler's textbook distinctly influenced the progress of medicine in another direction. It is related that a distinguished Baptist clergyman, who was close to Mr. John D. Rockefeller, read the first edition very carefully and noted the large number of diseases for which there was no specific or definite form of treatment. This was called to the attention of Mr. Rockefeller, resulting in the establishment of the Rockefeller Institute for Medical Research in New York City, which distinctly influenced medical investigation throughout the world.

During the 20 years of Dr. Osler's period in the United States, he stimulated many forward movements in medicine. As president of the Medical and Chirurgical Society of Maryland, corresponding to the State Medical Society, and by his frequent participation in the proceedings of the American Medical Association, he added interest and distinction to these new professional relationships.

He was a potent force in the organization of two medical organizations, the Association of American Physicians and the National Tuberculosis Association. He was privileged to train a group of young disciples who as teachers, investigators, and practitioners formed a "School of Osler" that profoundly influenced medical education and practice in America. He introduced several new syndromes of disease, that bear his name.

Dr. Osler had begun to feel the strain of his quadruple life as consulting physician, medical teacher, reviser of the textbook, and general bibliophile, so that he even talked of retiring. In all his American years, after leaving Canada, he had never become a citizen of the United States. At the same time he was proud of his British origin and too much of a lover of culture not to desire permanent contact with the older libraries and museums in which lay the chief food for his imagination.

During the early part of 1904, there were rumors of Dr. Osler's being called to Oxford as Regius Professor. While attending the annual meeting of the British Medical Association at Oxford in July 1904, the honorary degree of Doctor of Science was conferred on Dr. Osler by the University of Oxford. Shortly afterward came the formal offer by Lord Haldane, Prime Minister (it being a Crown appointment) as Regius Professor of Physic, and it was accepted.

Dr. Osler's last migration was deferred to May 1905, and during the following winter and spring he was kept busy attending farewell dinners and exercises in his honor. At all there was the warmest expressions of regard and affection from his many American colleagues.

During this period he also gave three valedictory addresses. At a dinner at the Waldorf Astoria Hotel, New York City, he said:

> I have had three ideals; first, to do the day's work well and not to borrow about tomorrow; second, to act the Golden Rule, as far as in me lay, towards my professional brethern and towards the patients committed to my care; and third, to cultivate such a measure of equanimity as would enable me to bear success with humility, the affection of my friends without pride, and to be ready when the day of sorrow and grief came to meet it with the course befitting a man.
>
> What the future has in store for me, I cannot tell—you cannot tell, nor do I much care, so long as I carry with me, as I shall, the memory of the past you have given me. Nothing can take that away.

Many honors came to Dr. Osler after he came to England, including the conferring of the Baronetcy at the Coronation of King George in June 1911; thus he became Sir William Osler. In 1918 he was elected President of the British Classical Association, the first time an English physician was so honored. His presidential address presented in May 1919 was "The Old Humanities and the New Science."

Like many others I early came under the spell of Dr. Osler, but did not meet him personally until June 1899 while attending the annual session of the American Medical Association in Columbus, Ohio. During the following six years there followed other meetings—at Atlantic City, Washington, visits to his clinics at Johns Hopkins, and to share with his many American

admirers in the general regret of his departure from Baltimore to become Regius Professor at Oxford, University.

I saw him but once after he went to England in 1905, and that was in July 1919. From some travel notes, a few leaves are taken to recall a happy day spent with Sir William Osler at his home in Oxford. My traveling companion, Colonel Louis A. LaGarde, Medical Corps, United States Army, and I arrived at the luncheon hour. Lady Osler was at the station with her Franklin car. There were two other visitors, Colonel and Mrs. Richard P. Strong; in civil life, Colonel Strong was Professor of Tropical Medicine at the Harvard Medical School.

We were soon at 13 Norham Gardens. Dr. Osler met us on the veranda with a greeting such as only he could give. He may have been Sir William to others, but to us he was still the same Dr. Osler we knew in the good days before he came to Oxford in 1905.

We were aware that the medical world, a few weeks before, had taken notice of his 70th birthday. At a brief and touching ceremony in London on July 11, with Sir Clifford Allbutt presiding, two memorial volumes had been presented to Dr. Osler.[1] Sir Clifford, who was Dr. Osler's brother Regius Professor (at Cambridge) had spoken of the memorable occasion as "One anniversary of many years of supreme service in two kindred nations and for the world," and added, "the first teacher of his day, and one of the most interesting and endowed minds and lovable characters in the story of our profession." With his more than 80 years, Sir Clifford had made jocular reference to his "youthful" colleague.

Colonel LaGarde and I, too, could have testified that age had dealt kindly with Osler, although he told us of having spent a week in bed after the birthday ceremony, in "another bout with the pneumonococcus." The black mustache had changed to gray, but otherwise the last 15 years seemed to have passed unnoticed. In the old-time twinkle of the eye, the winning smile, and the elastic, boyish activity, we saw the Dr. Osler his American friends had always known. Colonel LaGarde and Sir William were old friends. They had been born in the same year; so in their greeting there was much banter as to youthful appearance and the like. Sir William recalled the interesting work of LaGarde on ballistics and poisoned wounds,[2] done in the laboratory of Dr. William H. Welch in Baltimore 20 years before.

In Osler's many inquiries about American colleagues, one appreciated how he still entertained the warmest sympathies for America and her institutions, associated as they were with some of his happiest memories. One of his first questions was, "How

is my old friend (James T.) Priestley? Tell him I just picked up several fine old works of his ancestor, Joseph Priestley." He was interested to learn that the two grandsons of his friend (Joseph B. Priestley, M. D., now of Des Moines, Iowa, and James T. Priestley II, M. D., now of the Mayo Clinic, Rochester, Minn.) had entered the University of Pennsylvania, where once their distinguished ancestor was associated with the medical faculty.

We marveled at Dr. Osler's memory and knowledge of details of the various happenings in medical circles in America. He seemed to know so much about old friends and the service that each had rendered during the war period. Many had called on him; Oxford had evidently been the mecca for Americans during the previous five years. Lady Osler informed us that her maid had kept a record of the visiting Americans to whom tea had been served: The number was over 1,600.

Two special hospitals for the treatment of cardiovascular diseases and orthopedic conditions had been established in Oxford during the war, and a large number of American medical officers were stationed there from time to time. Lady Osler referred to the great pleasure it gave Sir William to have these fine young men about him. Many of us remember his particular affection for the younger members of the profession, and the medical officers who were so fortunate in being associated in service with Dr. Osler have treasured the memory of that experience.

Sir William was looking forward with interest and pleasure to meeting his many American friends the following year in New Orleans at the Annual Session of the American Medical Association.

After luncheon, we wandered about the beautiful garden and interesting home with its treasure store of books; later, under the guidance of Lady Osler, we saw a bit of the University that Oxford means to most of us. There is a particular charm about Christ Church, Merton, Magdalen, Pembroke, Balliol, Queen's, University, Oriel, and the other colleges that form Oxford University; some are mellow with age, while others belong to the newer group, but about all there cluster many interesting traditions of leading personages in English history. Lady Osler particularly desired us to visit the Latin Chapel in Christ Church Cathedral, where an interesting military wedding had taken place a year before, on June 29, 1918. Major Reginald Fitz of Boston had married Miss Phoebe Wright of Ottawa, Ontario, Canada; each was the child of old friends, and on leave from France at the time. Lady Osler told of the bride's being given away by Sir William, and of the reception and tea that followed on the terrace at "The Open Arms," the Osler's home at 13 Norham Gardens. "That they should have arranged for this wedding,"

said Cushing,[3] "was not only characteristic of the Oslers but. . . expressive of the warmth of feeling which England as a whole felt towards America."

There was a short visit to the Bodleian Library, with hardly more than a glimpse at its literary treasures. Dr. Osler had been named one of the curators soon after coming to Oxford in 1905. The duties must have been an attractive part of his new environment. Although he had to assume many new obligations during the war period, his interests and sympathies continued to be directed to promoting the highest ideals in medicine. His deep interest in the purpose of our visit was one example.

For a long time the idea had been in the minds of the leading clinicians and medical educators in the United States that the best means to elevate the standards of medical practice was to develop on a national scale a central qualifying board, expressive of the highest type of medical training in our country. As an outgrowth of this sentiment, the National Board of Medical Examiners of the United States was established in 1915.

With the close of World War I, the time seemed opportune to have a committee of the National Board in the United States make a comparative study of qualifying examinations as conducted by the Royal College of Surgeons, the Conjoint Board of England and the Triple Qualification Board of Scotland. The further object of the mission was to acquaint the members of these bodies with the aims and purposes of the National Board, with a view to bringing about some form of reciprocal understanding between their country and ours in matters of medical education on the basis of the examination conducted by the National Board. The committee consisted of Colonel Louis A. LaGarde and me. Colonel Victor C. Vaughan was detained at home because of the death of his son.

In previous correspondence, Sir William had been most helpful with advice as to the manner of approach and general procedure, and on this day he expressed gratification over the favorable impression that our mission had evidently accomplished. The committee had decided to include in its report a recommendation that the National Board extend an offical invitation for a British commission of three members, representing the qualifying bodies of England and Scotland, to come to the United States during the following year for a study of our leading medical schools and teaching hospitals and to attend a National Board examination in Philadelphia. The advice of Dr. Osler was again helpful in selecting the personnel of this proposed commission, and with his approval the names of the following men were submitted: Sir Humphrey Davy Rolleston, of the Royal College of Physicians; Sir Holburt J. Waring, of the Royal College of Surgeons and representing the Conjoint Board of England; and Sir

Norman Walker of the Royal College of Physicians, Edinburgh, and representing the Triple Qualification Board of Scotland. Sir William was most encouraging in his prophesies as to the outcome of these mutual visits. He recognized their far-reaching importance, not only in forecasting still further exchange of professional relations between the two English-speaking nations, but in advancing the higher ideals of world peace and human welfare.

Sir William and Lady Osler were making ready to leave the next day for a holiday on the island of Jersey. It had been a summer of peace and victory celebrations in England, but they were looking forward to this first opportunity for real relief from the great strain of the past five years. The war had brought the keenest sorrow to the Osler home, in the loss of an only son. This sadness did not find expression in words, although it was in the thoughts of all that July day. It was this quiet heroism in the aftermath of the great war, reflected in so many English homes, that more than all else engendered a stimulating hope for the future of that sturdy race.

The hour had come to say adieu. There was that in the words at parting—"Mighty glad that you boys came out"—and in the final wave of the hand which left a delightful impression of our visit to Oxford, to be more treasured with the passage of the years.

Soon after his return late in September to Oxford, he was called in consultation to Glasgow and Edinburgh. Because of the railroad strike he had to return from Newcastle to Oxford in an open car, which aggravated his "bronchitis" followed with bronchopneumonia, pleurisy, empyema, myocardial failure, and the end came quietly on the afternoon of December 29, 1919. There was but one Osler. He was fortunate to have his Boswell in Harvey Cushing who, in the two volume, *Life of Sir William Osler,* published in 1925, told a life story unequaled in all of medicine.

The dedication is significant:

> To medical students in the hope that something of Osler's spirit may be conveyed to those of a generation that has not known him; and particularly to those in America, lest it be forgotton who it was that made it possible for them to work at the bedside in the wards.

From this rich heritage of European culture and education which has been reviewed in brief retrospect, one may draw a parallel and proper relation to the remarkable evolution in medical education with the corresponding progress in research and medical practice in America since the turn of the century.

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It brought a newer concept of the origin of infectious diseases and closer relation of preventive and curative medicine.

An eminent American surgeon at that early period, a past president of the American Medical Association, spoke these words: "Prevention runs like a thread of gold through the entire fabric of medicine."

At the opening of the century there comes to mind the heroic figure of Walter Reed and his effective efforts in the control of yellow fever. Directly after the Spanish-American War, yellow jack had again raised its ominous banner on the rampage in Havana with a heavy toll each day of officers and men.

A yellow fever commission was organized, headed by Major Walter Reed, the other members including medical officers Kean, James Carroll, Jesse W. Lazear, and Aristide Agramonte. The first effort was to confirm the mosquito transmission of the disease, first expounded by Dr. Carlos Finlay 19 years before. Members of the Commission and two volunteers permitted self-inoculation by infected mosquitoes or were bitten accidentally, and each contracted yellow fever. Major Carroll became seriously ill, and Major Lazear succumbed to the infection, and thus became a martyr to science.

Largely due to the careful experiments by Lazear before his death, it was learned that *Aedes aegypti* mosquitoes to be infective must sting a yellow fever victim during the first three days of illness, and then before it can transmit its deadly load to infect another person, the virus must have a chance to ripen within the mosquito's body for at least 12 days.

One still gains a thrill in reading a letter written by Reed to his wife on New Year's Eve, December 31, 1900:

> Only 10 minutes of the old century remains; here I am sitting reading that most wonderful book "LaRoche on Yellow Fever" written in 1853; 47 years later it has been permitted to me and my assistants to lift the impenetrable veil that has surrounded the causation of this most dreadful pest of humanity and to put it on a rational and scientific basis. I thank God that it has been accomplished during the latter days of the old Century; may its cure be wrought out in the early days of the new.

The problem was solved after 8 months of faithful effort, and Camp Lazear was disbanded March 1, 1901. Armed with this new knowledge, Major Gorgas instituted needed sanitary regulations to control the mosquitoes, and Havana was freed of its age-old scourge in 90 days. Later, with this and other knowledge, Gorgas made the Panama Canal safe for the passage of commerce of the world, and the tropics became habitable for the white man. Since then yellow fever has been gradually brought under

world control, with the possible exception of the jungle areas in South and Central America, where the infected monkey continues to keep it alive.

Early in the century, eventful discoveries were reported from Germany. In 1905 Schaudinn, a prominent protozoologist in Berlin, announced the discovery of *Spirochaeta pallida (Treponema pallidum)* as the causative agent of syphilis, and in 1906 the discovery of the Wassermann reaction was announced by Wassermann, Neisser, and Bruck. In 1910 Ehrlich, as the result of his outstanding work in the study of the therapeutic effect of arsenical compounds in experimental syphilis, brought forth Salvarsan, or 606, which for a generation was the most potent and widely used drug in the treatment of syphilis. Ehrlich thus created a new science, that of chemotherapy.

During the first decade of this period a young investigator, Dr. Howard Taylor Ricketts of Chicago, began to shed new light on the origin and control of that group of infectious diseases which includes Rocky Mountain spotted fever and the several types of typhus fever. He took up the study of Rocky Mountain spotted fever in the spring of 1906 while on an enforced vacation in Montana. Dr. Ricketts promptly found that the disease was communicable to lower animals, and that a certain tick which occurred on a large number of animals in those regions, could by its bite transmit the disease from the sick to the healthy animal.

These observations opened a new aspect of problems both in the laboratory and the field, and after much hard work over a period of three years, he came to the conclusion that, in man, spotted fever depended simply on the accidental bite of an adult tick carrying active virus. The seasonal prevalence was explained, in that only adult ticks find their way to man and they occur only in the spring of the year. During the last year of his life, he demonstrated the immediate cause of spotted fever as a small bacillus, which he found in the blood of patients and in ticks and their eggs.

In recognizing the marked resemblance between Rocky Mountain spotted fever and typhus fever, Dr. Ricketts had become strongly impressed with the thought that the special knowledge and training acquired in this study would prove of great value in the study of typhus fever and its control.

Typhus fever has been one of the great epidemics of the world. Its devastations are recorded "on the dark pages of history, the pages that tell of war, overcrowding, want and misery."

After careful consideration, fully aware of the dangers and risks he would run, Dr. Ricketts decided to take up the study of typhus fever in the City of Mexico, and with his volunteer assistant, Mr. Russell M. Wilder, a senior medical student, began work in December 1909.

Before many weeks had passed, results of great importance were secured; it was found that typhus is different from Rocky Mountain spotted fever, although having many points in common; that Mexican typhus is communicable to the monkey; and that it may be transmitted by an insect *(Pediculus vestamenti)*, a species of louse. After several months they were able to confirm the discovery of a micro-organism, a bacillus, in the blood of typhus patients and in the insect.

While courageously and devotedly pushing this work to completion, Dr. Ricketts was stricken with typhus and died in Mexico City, May 3, 1910. Thus a young and noble career of great achievement and of large service to humanity came to a sudden and heroic end, and a new name was placed on the martyr roll of science. Many of the observations and discoveries in connection with this work of Dr. Ricketts had a much wider significance, particularly in the control, in World War II, of typhus fever and that group of infections now termed the rickettsial diseases.

During the Spanish-American War more soldiers died of typhoid fever than from battle casualties. One of the achievements of preventive medicine has been the protective vaccination against typhoid fever, largely instituted by Colonel Frederick F. Russell of the Army Medical Corps, so that in World War I there was not a single case of typhoid fever in the United States Army. Since then, through protective vaccination, typhoid fever has become a rare disease, the only problem remaining being the control of the typhoid carrier.

Malaria, another mosquito-born disease, has been brought under effective control in the United States during the past half century. This has been accomplished largely through elimination of the special mosquito vector (anopheles) by DDT spraying and destroying all pools and stagnant waters which are breeding places of the mosquito. While the anopheles mosquito still abounds in certain areas of the United States, the insect no longer spreads malaria as readily as formerly because there are fewer infected people and less opportunity for transmitting the disease.

However, on a world scale, malaria control continues to be challenged. It is being met by the organized efforts of the World Health Organization and the World Medical Association.

In the malarial region of Asia, the Near East, and Equatorial Africa, the anopheles mosquito will infect several million people each year, of which at least one million will die. The effect will not be confined to the areas involved, because malaria has a high impact on the world's economy and also is the major cause of poverty and malnutrition.

A new era in American medicine, particularly in the treatment of infectious diseases occurred with the introduction of the antibiotics, just preceding World War II. The first group were the sulfonamide drugs, originating in Germany, but greatly purified by manufacturers in this country, which reduced the mortality from pneumococcic pneumonia and other acute infections due to streptococci and staphylococci to a marked degree.

The second group of antibiotics, of which penicillin was the first example, were all products of lower micro-organisms such as molds, fungi, and soil bacteria.

The story of penicillin, discovered in 1928 by Dr. Alexander Fleming, a London pathologist, constitutes another romance in medicine. He prepared the material from a common soil mold, and after it was identified by the American entomologist, Thom, as *Penicillium notatum,* he named the product penicillin. The successful isolation and purification of penicillin, and the clear-cut proof of its antibiotic action and clinical value, with assay and unit of dosage, was the work of Dr. Howard W. Florey, and Dr. Ernest Boris Chain at Oxford.

The onset of war expedited the development of penicillin, and the great need for its mass production was promptly met by enterprising drug manufacturers in this country. The supervision of its production on a large scale and careful distribution, to the Armed Forces and, especially, civilian hospitals, were under the direction of a Committee of the National Research Council; all of which was indicative of a broadly conceived program of study and critical research that placed our knowledge of penicillin on a sound basis—a sound scientific and clinical basis. It soon came into extensive use in the military hospitals of all the Allied Nations, and may well be accredited with a prominent part in winning the last war. Later, it became generally available for civilian hospitals in this country, and the dramatic results everywhere were in keeping with the high expectations of the earlier studies.

As penicillin was still powerless in certain bacterial infections, search for other weapons led to discovery of a number of other antibiotics, all of which have been developed in American laboratories. Waksman discovered streptomycin in 1944, and it became an effective remedy in tuberculosis. Chloro-

mycetin, developed in 1947 by Burkholder in the Detroit laboratories of Parke, Davis & Company, has been specially effective in typhus and the other rickettsial diseases. Benjamin M. Duggar and his associates at the Lederle Laboratories in Pearl River, N. Y., discovered, tested, and produced Aureomycin, later Achromycin, which has given remarkable results in the treatment of brucellosis, amebic dysentery, and such virus diseases as atypical pneumonia, psittacosis, and the rickettsial diseases. Terramycin, one of the newer antibiotics, has proved to have a still broader spectrum of effects among many of the microorganisms in the bacterial, viral, rickettsial, and protozoan groups.

While penicillin is extensively used in a large group of infections, the two outstanding results are its use in subacute bacterial endocarditis and the venereal diseases. Before the introduction of penicillin, subacute bacterial endocarditis, a prolonged inflammation of the heart valves, was invariably fatal. By the use of large doses of penicillin, a majority of these cases now are cured, and it is acknowledged by leading internists that the new treatment of subacute bacterial endocarditis is, barring insulin, the greatest therapeutic triumph of this century.

It has had an equally remarkable therapeutic effect in the treatment of venereal diseases. The former methods of treatment required several years for disappearance of symptoms, but now with adequate dosage and prompt diagnosis, it is possible to render the infected person noninfective after one or two days, and a disappearance of all symptoms of the disease within two or three weeks. The incidence of congenital syphilis after effective prenatal treatment of the mother has been reduced to a minimum; likewise the admission of chronic forms of the disease in mental hospitals has been lowered greatly. There is reason to say that syphilis is on the way out and to hope that ere long the curtain will drop on this the darkest shadow in the land.

Within recent years, protective vaccines, such as the Salk vaccine for poliomyelitis and a vaccine for the Asian strain of influenza have been produced. Our knowledge of the viruses and virus diseases has been greatly advanced, as, since the turn of the century, has our knowledge of the noninfectious diseases. It may well be said that the era of Pasteur is still with us.

The closing years of the last century saw a great discovery in physics—a discovery which was to be of incalculable value to medical science—the discovery of x-rays by Wilhelm Conrad Röntgen, Professor at the Physical Institute of the University

of Würzberg. Medicine profited further from other great advances in physical science—particularly the discovery of radium by Pierre and Marie Curie, first announced in July 1898.

Largely through the experience with scurvy and beriberi; attention was directed to "indispensable ingredients in the food." In 1912 Casimir Funk published an article on "Etiology of Deficiency Diseases," and proposed the name "Vitamine" for these deficiency substances. Since then a vast literature has apperaed, with a classification into vitamins A, B_{1-12}, C, D, E, and others, each deficiency being connected with a special disease process. Closely connected with these investigations, there has developed an increasing knowledge of the internal secretions, their physiologic functions, and relation to definite disease conditions.

During the third decade of this period, two remarkable achievements came in American medicine in the treatment of diabetes mellitus and of pernicious anemia, both classified as deficiency diseases.

The story of the final conquest of diabetes may best illustrate the integration of scientific research along many lines and finally lead to results of greatest practical importance. It may further be compared to a Greek relay race—where each runner lands the torch to the relay, and when the final race is won, full credit is due to each who kept the light burning all along the way. Extending back over a hundred years it had its beginning in Liebig's laboratory at Giessen and the study of the hydrocarbons, the recognition of the sugar excreted as glucose, the discovery of a special test with a solution of copper sulfate by Fehling; the contributions by Claude Bernard, the great French physiologist, on the glycogenic function of the liver; the demonstration of special islets in the pancreas by Langerhans in 1854; the production of experimental diabetes in dogs after removal of the pancreas by von Mering and Minkowski in the eighties; the demonstration in 1904 of special pathologic changes in the islands of Langerhans, by Opie, the American pathologist; and crystallized by the naming of the hypothetical, as yet undiscovered hormone, insulin, in 1913 by Sharpey-Shafer, the English physiologist.

Efforts were made by careful investigators to obtain alcoholic and acidulated extracts of the island tissue of the pancreas, and when the same were injected into depancreatized dogs, the glycosuria diminished and the general condition improved. The prize in the race, however, was reserved for three Canadian physicians, Banting, Best, and Macleod, of Toronto, who in 1922 were able to report the successful clinical use of insulin in patients with diabetes. A number of modifications have since

been made in insulin preparations, permitting less frequent administration of the same, and the list of permissible diabetic foods has been greatly increased, so that the diabetic patient of today has a wide choice of diet and can live a normal life of many years.

During the first 25 years of this century, the patient with pernicious anemia could look forward to only one termination, as patients rarely lived a year after the first symptoms. This disorder of the blood-making system, in which the red cells are greatly diminished and the maturing factor of the same is deficient, has baffled investigators as to its origin and specific treatment ever since it was first recognized by Addison more than 100 years ago. Whipple in 1921 published the results of repeated bleedings of dogs, producing a condition of the blood state similar to that observed in the blood of patients with pernicious anemia. He found further that by feeding these anemic dogs certain foods rich in protein, such as liver, the blood condition rapidly returned to normal. These experiments formed the basis of the contribution of Minot, Murphy, Castle, and associates in Boston, in establishing the liver treatment of pernicious anemia.

It was evident that the absence of a constituent of normal gastric secretion in pernicious anemia patients interfered with blood formation. This "intrinsic factor" interacts with some constituent of food (extrinsic factor) to produce an active anti-anemia principle which is stored in the liver. The liver extracts combine with the intrinsic principle, and when given at appropriate intervals, maintain the blood of the pernicious anemia patient at a normal level. Since this is clearly a deficiency disease, it is necessary to continue the liver treatment more or less continuously for many years. In recent years preparations of folic acid and vitamin B have been used with effective results in special types of pernicious anemia.

Since the turn of the century, very significant progress has been made in the diagnosis and treatment of cardiovascular diseases. Early in this period appeared the name of a brilliant general practitioner, Dr. James Mackenzie, who distinctly advanced our knowledge of the diseases of the heart and blood vessels during the first three decades of the century. His medical life forms an interesting story. After graduation from the University of Edinburgh and a year as resident in the Royal Infirmary, he entered general practice at Burnley, a factory town in northern England. In the busy life of a general practitioner, his keen mind became centered on two definite objects—first, the understanding of the mechanism of symptoms, and second, the understanding of their prognostic significance.

These were the simple resolutions and definite aims which led to the achievements and great success that came to Mackenzie in later years. He began to study the symptoms in every patient, and an accident directed his attention and special interest to diseases of the heart and circulation. A woman patient in labor, died suddenly of heart failure. This led him to studying the circulatory condition of women, before, during, and after pregnancy. He noted particularly pulse irregularities as an abnormal sign, and soon recognized two types—dangerous and not dangerous. He began to make pulse tracings by means of the old Dudgeon's sphygmograph of every patient and endeavored to analyze them. Soon he began the study of the venous pulse in the jugulars, which led to the ink polygraph that bears his name. By this he was able to make simultaneous graphic tracings of the jugular venous pulse, the carotid pulse, and the apex beat of the heart. By many, this discovery is regarded as the greatest contribution that Mackenzie has made to medicine.

He soon noted so-called "missed beats," which he explained as preventricular contractions and named them extrasystoles. Among the dangerous forms of irregularities was a type in which the patient usually died in 5 or 6 years, and all seemed to be victims of heart failure, frequently the result of rheumatic fever. In a patient with mitral stenosis and accompanying congestion of the liver, he noted in auscultation that the presystolic murmur was absent; the thought came to him, that the "auricle had stopped beating." He called this "paralysis of the auricle," and the arrhythmia, auricular fibrillation. He noted further that digitalis slowed the fibrillation and relieved the decompensation.

His ideas were not readily accepted by leaders of the profession, and his early papers and writings were refused by leading medical journals. In 1902 he published his book, *Study of the Pulse,* which gained great favor in Germany and America long before the giants of the English profession would even glance at it.

After a visit by Mackenzie to America and Europe, many leaders came to Burnley, but few of his own country, with the exception of Sir William Osler, Sir Thomas Clifford Allbutt, and Sir Almroth Edward Wright. So this general practitioner decided to go to the giants, and in 1907, at 54 years of age, he moved to London and opened an office in Harley Street. During his first year he saw but few patients and earned only 114 pounds, or about $500. There were no hospital appointments or opportunities to teach. However, he was not discouraged, and it gave him the time to complete the publication of his great work, *Diseases of the Heart and Blood Vessels,* which established him as a cardiologist. This brought about a great awakening among the giants of the English profession. His annual income in-

creased to 1,000 pounds sterling; he received important hospital appointments; was elected to Fellowship in the Royal College of Physicians of London and the Royal Society of Medicine, then elevated to knighthood.

He was referred to as a wizard, which he resented, because he considered that his ability to diagnose and prognosticate was due to knowledge of essential symptoms and warned "That no instrument, stethoscope, polygraph, or electrocardiograph, could replace mind and reasoning power of the doctor himself."

In 1903, Einthoven of Leyden introduced the string galvanometer, now known as the electrocardiograph, to the scientific world. Mackenzie was never very enthusiastic about it, but he was greatly interested in the studies of his distinguished pupil, Sir Thomas Lewis, who first introduced the electrocardiograph into hospital service in London in 1906. However, the electrocardiograph helped to establish Mackenzie as a wizard, as it proved his tracings and interpretations to be correct.

At the close of World War I, in which he served as special consultant in chest diseases, he left his consulting room in Harley Street and an income of more than 8,000 pounds a year, at 65 years of age, to return to general practice in the old university town of St. Andrews, Scotland, a short distance from his native Perth, in order to better study the earliest symptoms of disease, the significance of the same, and the mechanisms of its production. On a personal visit a few years later, I asked Sir James why he had selected St. Andrews and he answered, "I wanted to practice in a community where 95 per cent of the people were born, lived, and died there."

In 1919 he established the St. Andrews Institute for Clinical Research, and here, in the wards of the adjoining Andrews College Hospital, began the study of the early signs of disease at all ages. In July 1922, I was privileged to visit Sir James at St. Andrews, and had the opportunity to attend the weekly outpatient clinics where the patients were brought in by the practitioners of the town; it was easy to recognize the stimulating influence of these conferences on the medical practice of the community. As I stood in the long consulting room after a visit throughout the Institute, I felt that it all accorded so well with the mind and spirit of the man who acted as my guide.

In one of the clinical discussions, the subject of hypertension was brought up—and suddenly Sir James grasped the lapel of my coat and said, "I say Doctor, you are going crazy in your country on blood pressure—and you don't know a dum thing about it, now do you"? Here, 35 years later, hypertension is still a problem unsolved.

Two years later, attacks of severe angina gradually made it necessary for Sir James to give up professional work and his death came on January 25, 1925. His distinguished disciple, Sir Thomas Lewis, said in tribute, "The greatest of his work lay in the fact that he so developed and simplified the method of approach as to bring it within the scope of the general practitioner."

The classic contribution of Dr. James B. Herrick in 1912 defined coronary thrombosis as a clinical entity, which was readily recognized by its symptom complex, frequency amenable to therapy and recovery. Dr. Fred Smith, an associate of Dr. Herrick, by ligation of the coronary artery in dogs produced experimental coronary thrombosis and resulting myocardial infarction, as shown in electrocardiograms. Herrick, with other American clinicians, added a new chapter in internal medicine and distinctly advanced our knowledge of myocardial infarction and degenerative heart disease.

The judicious use of anticoagulant drugs such as dicumarol and heparin has distinctly changed the course of illness in coronary heart disease, as well as the extent of damage to the heart muscle. With the better control of syphilitic infection this form of heart disease has become much less frequent.

It is hoped that the several protective measures instituted to control rheumatic fever, will distinctly lower the incidence of rheumatic heart diseases. Congenital heart disease is now being successfully treated by the surgeon.

The increasing recognition and incidence of coronary heart disease has stimulated intensive research in the genesis of atherosclerosis as it occurs in the coronary, as well as the renal cerebral and peripheral arteries. It has successfully been produced experimentally in rabbits and chickens by the use of cholesterol or certain food substances with high cholesterol content. In consequence there is a growing concept that the fat content of the average present-day diet is a significant factor in the cause of human atherosclerosis.

Recently a group of cardiologists[4] summarized and evaluated the evidence with the conclusion that, "To date there is no incontrovertible evidence for such a relationship; nevertheless, a strong case is developing to suggest that the nutritional status of an individual is an important environmental factor in the etiology of this disorder. The total fat and the type of fat in the diet are among the nutritional factors particularly involved."

Great milestones have marked the evolution of American surgery during the past half century, too numerous and complex to outline fully. Thoracic surgery, or surgery of the chest, came

into prominence early in the third decade. The successful removal of large numbers of foreign bodies from the heart cavities during World War II, developed a technic and experience that led to still greater extension of cardiovascular surgery following the war.

The congenital malformations of the heart and larger blood vessels are now effectively relieved by open-heart surgery. Great progress has been made in the surgical relief of chronic defects of heart valves—as mitral stenosis—accompanying rheumatic heart disease. The operation of valvotomy is now well established with remarkable restoration of physiologic function—patients being rendered more comfortable, free from distress, and often able to return to work. Remarkable results also have been obtained in the use of arterial grafts in aneurysm and other forms of arterial disease.

The most exciting recent development in American medicine was the announcement nine years ago by Hench, Kendall, and Reichstein of the discovery of a new hormone of the adrenal cortex, called cortisone or compound E, and of a pituitary adrenocorticotrophic hormone (ACTH), and their dramatic effect in the treatment of rheumatoid arthritis. They have been equally effective in the allied group of disorders, the so-called collagen or connective tissue diseases, which include rheumatic fever, periarteritis nodosa, scleroderma and lupus erythematosus. They present a new therapeutic approach in that the pathologic physiology of this group of diseases is rendered potentially reversible, and have further demonstrated the importance of the adrenal cortex in body metabolism. With the introduction of newer steroids and as the tolerance dosage becomes better established with a clearer understanding of its therapeutic limitations, the future of these new remedies is most promising.

We have all been impressed by the interesting work of Dr. Hans Selye of Montreal in the physiology and pathology of exposure to stress. The concept of a general adaptation syndrome and resulting diseases of adaptation will direct our thinking of disease conditions incident to living in this strenuous age.

In reviewing these epochal events in American medicine, it will be evident that medical education, in order to keep in tune with new discoveries and changes in medical practice, must have undergone an equally remarkable evolution in methods of training during the past half century. One can look back now and see the great drama that took place in medical education in America. Within a comparatively few years the number of commercial medical schools was strikingly reduced, university medical schools were organized, the length of the medical course was markedly increased, the number of medical students dimin-

ished, and there began that evolution that has advanced medical education in America so that it is the peer of that of any country in the world. It must ever be to the credit of the American physician, acting through the American Medical Association, who saw the need of using the constantly growing knowledge and was willing to make the sacrifices that go with change.

There was further supervision of the phenomenal expansion of graduate teaching in medicine. Now, practically all medical graduates have at least a year's internship and hospital residencies have steadily increased with the establishment of certifying boards in the different medical and surgical specialties. These, with fellowships in the different fields of clinical medicine have offered increasing opportunity for training and teaching.

So rapid were the developments in the practice of medicine itself, that it speedily branched off into specialties. One after another they flared on the horizon, some born overnight, self-styled or self-anointed as it were, but these, too, have been brought under supervisory control by the organization during 1933-1934 of the Advisory Board for Medical Specialties, which determines the formation of new boards of certification and, in co-operation with the Council on Medical Education and Hospitals, American Medical Association, gives approval to the residency and graduate training required for certification by the individual specialty boards.

The remarkable discoveries and achievements of American medicine during this period are largely due to physicians and surgeons adequately trained in special fields of research or practice. For a while, with the growth of specialism, it seemed as if the family physician of the past was doomed, but gradually the training of the specialist has been pushed up into the hospital years, and the undergraduate curriculum in our medical schools is now being arranged to provide a broad well-rounded training for the "basic" doctor who with additional graduate experience will emerge as the general medical consultant of the future, the cultured family physician who will best be able to determine when specialized skill and knowledge is needed for the welfare of the patient.

Because of world-wide changes, it must be evident to all that the challenge and responsibility for the future progress of world medicine rests largely with the medical schools, research institutions, clinicians, practitioners, and public health workers here in America. However, if this high place in world medicine in to be maintained, it is timely to recognize that American medicine in the future will require the recruitment of superior students, the organization and integration of the community to

supply the opportunities of advanced medical education, and continued generous financial support.

It has been well said that "the past is but a prologue of the future." There are still many unsolved problems in medicine. In a recent two-volume publication by the American Foundation entitled, *Medical Research: A Midcentury Survey,* the following unsolved clinical problems in biologic perspective are listed: cancer; infertility; atherosclerosis; hypertension; rheumatic syndrome; tuberculosis; nature of viruses and virus diseases; alcoholism; and the biology of schizophrenia and human behavior. The continuing increase of an aging population and greater incidence of chronic or long term diseases is profoundly influencing the character of medical practice. The newer fields of aviation and atomic medicine present a further challenge to the medical student, research worker, and practitioner of tomorrow.

With a due appreciation of the great heritage of service and opportunity that we now enjoy, we pray for that wisdom broad and deep to guide aright the destiny of medicine in the days ahead.

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PROPOSAL FOR A CERTIFIED STANDARD FOR USE IN HEMOGLOBINOMETRY

Second and Final Report

R. KEITH CANNAN, *D. Sc.*

IN 1953 the Hematology Study Section of the National Institutes of Health requested the Division of Medical Sciences of the National Academy of Sciences–National Research Council to explore the possibility of establishing a hemoglobin standard for general use throughout the country. In response to this request, the Division in 1954 organized an Ad Hoc Panel for the Establishment of a Hemoglobin Standard under its Subcommittee on Blood and Related Problems.

Dr. George E. Cartwright, School of Medicine of the University of Utah, Salt Lake City, Utah, accepted the Chairmanship of the Panel. Its members were Dr. David L. Drabkin, University of Pennsylvania Graduate School of Medicine, Philadelphia, Pa.; Lt. Col. William H. Crosby, Walter Reed Army Institute of Research, Washington, D. C.; Dr. George Brecher, National Institutes of Health, Bethesda, Md.; Dr. Wallace R. Brode,* National Bureau of Standards, Washington, D. C.; Dr. Israel Davidsohn, Mount Sinai Hospital, Chicago, Ill., representing both the College of American Pathologists and the American Society of Clinical Pathologists; and Dr. Abram H. Neufeld, representing the National Research Council of Canada. In 1956 Mr. John H. Gould, National Bureau of Standards, succeeded Dr. Brode; and in May, 1957, Dr. Bradley E. Copeland, New England Deaconess Hospital, Boston, Mass., and Dr. Donald E. Brown of the Hackensack Hospital Association, Hackensack, N. J., succeeded Dr. Davidsohn as representatives of the College of American Pathologists and the American Society of Clinical Pathologists, respectively. The Panel also was fortunate in having the co-operation of Dr. Earl J. King of the University of London, Postgraduate Medical School, London, England, who has given his full support to this undertaking.

From the Division of Medical Sciences, National Academy of Sciences–National Research Council, Washington 25, D. C. This study was supported by a grant from the National Heart Institute, National Institutes of Health, Bethesda, Md., Contract Number H-2145.

*Dr. Brode is now Science Adviser to the Secretary of State.

Most routine methods of clinical hemoglobinometry depend upon the photometric measurement of a blood sample after quantitative conversion of the hemoglobin which it contains into one or another of its derivatives. For the standardization of such a procedure there is needed a color standard which, when measured in the photometer and cuvette in routine use, will establish the relation between instrument reading and concentration of the particular hemoglobin derivative. This relation then can be used in converting instrument readings for unknown samples of blood to concentration of hemoglobin by the use of Beer's law or by construction of a calibration curve.

The problem, however, is complicated by the fact that several methods of analysis involving conversion to different forms of hemoglobin are in common use. Each of these methods should have its own standard. Because a multiplicity of standards is neither desirable nor practicable, the Panel decided, early in its deliberations, to select only one method of analysis for which a suitable direct standard would be developed. It should be pointed out, however, that this procedure does not preclude the use of the standard for the indirect calibration of another method. All that need be done is to construct a calibration curve based on the measurement of a small series of *normal* blood samples by the standardized method and also by the method which the analyst prefers to adopt for routine use.

In the opinion of the Panel, the most significant contribution which could be made to the refinement of clinical hemoglobinometry would be the widespread adoption of a single method of analysis. Failing this, the indirect calibration of other methods with the chosen method offers the only simple photometric means for the comparison of data. The procedure, however, is subject to error if the blood sample contains significant amounts of certain of the abnormal forms of hemoglobin. For example, methemoglobin and carbon monoxidehemoglobin are convertible quantitatively to cyanmethemoglobin, but not to oxyhemoglobin.

The Panel reviewed the several photometric methods in current use and came to the conclusion that the procedure involving the measurement of hemoglobin as cyanmethemoglobin was the most promising. It offered the following advantages:

1. A simple and accurate procedure has been devised by Drabkin and Austin[1,2] involving the addition of a single reagent to the sample of blood;

2. The method has been adopted by the U. S. Army after extensive field trials;[3]

3. All forms of hemoglobin likely to occur in circulating blood, with the exception of sulfhemoglobin, are determined by the method;

4. The color is suitable for measurement in filter-type photometers as well as in narrow band spectrophotometers because its absorption band in the region of 540 mμ is broad and relatively flat; and

5. The U. S. Army has had extensive experience in the use of solutions of cyanmethemoglobin as direct standards and has found these to be satisfactory.[3] The U. S. Army standards have remained unchanged in optical density for extended periods when stored at refrigerator temperatures, provided bacterial contamination was avoided.

On the basis of this evidence, the Panel decided to develop a certified solution of cyanmethemoglobin as a standard, and to promote an extensive field trial of its suitability.* A preliminary report of its recommendations and plans[4] appeared in a number of scientific and technical journals in 1955. This report outlined recommendations of the Panel, described arrangements for the preparation and distribution of certified standard solutions of cyanmethemoglobin, and invited cooperation in an extensive field trial of the use of the standards and of the recommended method of analysis.

More than a thousand laboratories volunteered to co-operate in the trial sponsored by the National Research Council. Distribution of the standards was made with the assistance of the College of American Pathologists, the National Association of Clinical Laboratories,** the Walter Reed Army Institute of Research, and the National Research Council of Canada. The laboratories not only received descriptions of the procedures for the use of the standards to calibrate photometers, but also directions for the routine determination of hemoglobin in the form of cyanmethemoglobin.

The results of the study were most gratifying. The need for, and the ready and grateful acceptance of, a simple method for the standardization of hemoglobinometers was apparent. The recommended method of analysis likewise was well received. At the onset of the field trial study only seven per cent of the co-operating laboratories had been determining hemoglobin as

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*Proteins are not regarded generally as highly stable in dilute solution, even if sterile. In spite of the experience of the U. S. Army the Panel hesitated to adopt a standard to which theoretical objection might be taken and explored other more stable materials. These included colored glasses and solutions of pigments so prepared as to approximate the absorption by cyanmethemoglobin of the spectral transmission of the filters, prisms or gratings employed in photometers and spectrophotometers. These alternatives were rejected because (a) no suitable mixture of pigments suggested itself, (b) it would be necessary to provide a series of glass standards to match the sizes and shapes of commonly used cuvettes, and (c) for some instruments the glasses would also have to match the lens effect of the round cuvettes and their contents.

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cyanmethemoglobin. At the time of the last report, two thirds of the co-operating laboratories were using this method.

In the first field trial, the standard solutions were prepared from crystalline hemoglobin by Dr. David Drabkin. Three solutions in carefully determined concentrations of approximately 60, 40, and 20 mg of hemoglobin per 100 ml were distributed. The optical densities of the final solutions were confirmed independently and a continuing control on stability was maintained in the laboratories of Dr. Brecher, Mr. Gould, Col. Crosby, Dr. King, and Dr. Neufeld. Agreement having been reached on the optical density values, the hemoglobin concentrations of the standards in mg per cent were computed from the optical densities, assuming that the extinction coefficient of cyanmethemoglobin per milligram-atom of iron (55.85 mg) per liter is 11.5 and that the pigment contains 0.335 per cent of iron.

Two problems were encountered during the course of the field trial study. The first of these was the growth of certain microorganisms observed in some samples in spite of the presence of cyanide. This made it necessary to prepare and to maintain the solutions under sterile conditions. The second problem was a change, unpredictable in degree and not reported by all checking laboratories, of two to six per cent in the optical density six to nine months after distribution of the standard. Samples from each lot were found to have undergone varying degrees of change, mostly fading, which was compensated in some samples by a comparable increase in turbidity. The standards prepared and distributed by the U. S. Army in its earlier field trial had remained unchanged in optical density for three years. Inasmuch as these solutions had been prepared directly from whole blood or from washed red cells, it was suspected that the manipulation involved in the preparation of the crystalline hemoglobin for the National Research Council standards might have reduced the stability of the pigment. Therefore, a new standard was prepared from washed cells. The new standard was modified further by increasing the concentration of cyanide, both because some previous preparations with such higher concentrations had shown greater stability and because the growth of most organisms would be limited by the higher concentration of cyanide.

Because the percentage change in optical density of the first standards was greater with increasing dilution of the hemoglobin pigment, and because cyanmethemoglobin solutions follow Beer's law, the second standard was distributed in only the most concentrated (60 mg per cent of hemoglobin) of the three dilutions.

The second group of standards, modified as outlined above, was distributed in July and August of 1956. Their stability was determined in the laboratories of Dr. Drabkin, Dr. Brecher, Mr.

Gould, and Col. Crosby. The stability was satisfactory for at least nine months from the time of preparation, no change of more than two per cent in optical density being observed.

The members of the Panel have concluded that solutions of cyanmethemoglobin, when prepared, calibrated and handled properly, are acceptable as standards for hemoglobinometry. They recognize that such standards are not ideal in all respects. Until better standards can be developed, however, they are of the opinion that the availability of this reagent will simplify greatly the calibration of hemoglobinometers and will increase greatly the accuracy of hemoglobinometry over previously employed practices.

Finally, they encourage further independent investigation in the hope that an even better standard may be developed, particularly one with improved stability and more certain maintenance of sterility.

The National Research Council supplies of the standard cyanmethemoglobin solution are now exhausted and no further production is planned under the auspices of the Academy–Research Council. However, standards are now available from several commercial sources. The NAS-NRC has recommended the establishment of a program of certification of commercially produced cyanmethemoglobin standards to determine conformance with the specifications it has established. In response to the need for the establishment of such a program, as defined by the NAS–NRC, the College of American Pathologists* has arranged for certification through the facilities of the laboratory of the American Medical Association in Chicago. On the basis of data obtained through this laboratory, the College of American Pathologists will certify whether commercially produced standards which have been submitted comply with the specifications established by the NAS–NRC.. *All users are urged to insist that the cyanmethemoglobin standards they purchase commercially carry the certification label of the College.***

Detailed instructions for the preparation of the standards have been published by Crosby.[5] Producers of the standard or instrument manufacturers may obtain technical details on the adaptation to and use of the standard in the various hemoglobinometers by writing to the Division of Medical Sciences of the National Research Council.

The final recommendations of the National Research Council Ad Hoc Panel on the Establishment of a Hemoglobin Standard are as follows:

*College of American Pathologists, Prudential Plaza, Chicago 1, Ill.

**In Canada discussions are now taking place in order to make one national laboratory responsible for the production and certification of the standard solutions.

1. That cyanmethemoglobin be adopted as a standard in clinical hemoglobinometry.

2. That the standard be characterized spectrophotometrically on the basis that the extinction coefficient of one milligram atom of iron (c = 1 mg atom of iron per liter, d = 1 cm) in the form of cyanmethemoglobin at a wavelength of 540 mμ is 11.5.

3. That 0.338 per cent (w/w) be accepted as the iron content of hemoglobin (molecular weight of 16,520 per gram atom of iron in accordance with the recent recommendation of the Protein Commission, section of Biological Chemistry of the International Union of Pure and Applied Chemistry,* and that a factor of 1,652 be used in calculating hemoglobin in mg per 100 ml from millimoles per liter.

4. That the standard be distributed as a single concentration of not less than 55 mg of cyanmethemoglobin per 100 ml.

5. That solutions be distributed in brown glass containers and in sterile condition.

6. For the present it is recommended that solutions should be used as standards for a period not to exceed nine months from the time of preparation. This dating period is based upon the results of the National Research Council field trial. As experience accumulates with commercially prepared samples, an extension of the dating period may well be found to be justifiable.

7. That the standard be prepared from either crystalline hemoglobin or washed erythrocytes.

8. That commercial producers of the standards submit representative specimens from each lot to the College of American Pathologists, Prudential Plaza, Chicago 1, Ill., for certification (a) that the concentration of cyanmethemoglobin is within ± 2 per cent of the value stated on the label; (b) that the solution is substantially optically clear; and (c) that it is microbiologically sterile.

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*International Union of Pure and Applied Chemistry; headquarters are at Basel, Switzerland.

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KNEE INJURIES IN MILITARY PERSONNEL

"Knee injuries in actively serving military personnel are an important cause of loss of manpower, both from a standpoint of prolonged convalescence and permanent partial disability. The age group of the serving soldier is, we think, responsible for the frequence with which we find knee injuries in these men. They are a young, healthy, vigorous group, who subject themselves to frequent and strenuous trauma in their daily training and are prone to engage in vigorous sports as well. In judging the final results of treatment in post-operative cases, one must not accept too readily the statistics on civilian personnel, and attempt to apply them to military patients. A civilian patient who may be considered to have a completely satisfactory recovery, allowing him to meet all the demands of a normal civil life, may from a military viewpoint not be considered fit to undergo the strains of modern military training or battle. It is interesting to note that most of the acute knee injuries seen, especially those involving tears of the menisci, are sustained either in training or on the sports field, and are not due to the motor vehicle accident, which supplies so many of the traumatic cases seen in the surgical wards of our army hospitals in peacetime."

—G. W. CHAPMAN, Maj., R. C. A. M. C.
in *Canadian Services Medical Journal*
p. 486, Sept. 1957

Clinicopathologic Conference

U. S. Naval Hospital, Chelsea, Mass.*
U. S. Naval Station Hospital, Naples, Italy**

JAUNDICE AND FEVER

Case 1.

Summary of Clinical History. A 30-year-old Caucasian was admitted to the hospital because of general malaise and vomiting. Two days previously he had noted the onset of fever followed by increasing weakness and vomiting. Anorexia was prominent, and he believed his skin was getting yellow.

Physical Examination. The patient was an acutely ill man who appeared apprehensive and toxic. The skin and sclera were icteric. The heart and lungs were normal. The liver was palpable at the costal margin and was moderately tender. The spleen was just palpable. His temperature was 104.2°F, and his pulse was 86 per min., and the respiratory rate was 20. Blood pressure was 86/54 mm Hg.

Laboratory Studies. The hemoglobin was 13.5 grams per 100 ml. The white blood cell count was 8,000 per μl, with 49 per cent neutrophils, 40 per cent lymphocytes, 2 per cent monocytes, 2 per cent eosinophils, and 7 per cent basophils. The urine contained bilirubin. Dark-field examination of serum and urine for spirochetes was negative.

Course in Hospital. The patient continued to vomit and was given fluids intravenously. He ran a spiking temperature (104°F) and maintained a relatively low pulse (under 100). The vomitus

*Capt. Cecil D. Riggs, MC, USN, Commanding Officer. From the Laboratory Service, Capt. Francis J. McMahon, MC, USN, Chief.
**Capt. Marcy Shupp, MC, USN, Commanding Officer.

became brown in color and was positive for occult blood. In the next four days the patient developed severe hiccuping, intermittent in character but very uncomfortable. The liver remained palpable and tender. The white blood cell count rose to 15,000 per μl with 95 per cent neutrophils and 5 per cent lymphocytes.

On the fifth hospital day the patient's temperature dropped from 103° to 98°F. His pulse rose to 100. He stated that he felt much better and that he was hungry. He was allowed clear fluids and soft custard. He had no further vomiting. That evening, although confined to bed, he got up, and sat for awhile. Later he returned to bed and while there he sat up suddenly because he could not breathe and felt cold. He went into shock rapidly, developed dyspnea, and expired.

Case 2.

Summary of Clinical History. A 34-year-old plane captain was admitted to the hospital because of fever, malaise, and vomiting. Jaundice was noted on the day of admission.

His plane had one crew member admitted to the sick list (case 1) and a third recovering from infectious hepatitis at the U. S. Air Force Station Hospital, Dhahran, Saudi Arabia. All the crew members had been inoculated against yellow fever. The crew were exposed to rats. The plane, normally based at Dhahran, had departed with the same crew, for Aden, British Protectorate, one month prior to the patient's admission to the hospital. The plane crew remained in Aden four days before returning to Dhahran. Five days later the plane took off for Jidda, Saudi Arabia, and Asmara, Eritrea. In the next few days the plane flew between Cairo, Egypt, and Dhahran, Saudi Arabia. Sixteen days prior to the patient's admission to the hospital the plane and crew took off from Dhahran for Massaua, Eritrea, then going to London via Cairo, Beirut, and Naples.

Physical Examination. The patient appeared acutely ill, jaundiced, and unusually toxic. The heart and lungs were normal. The whole abdomen was tender. The liver edge was just palpable below the costal margin on deep inspiration and was tender. The spleen was not palpable. The temperature was 100.8°F; the pulse, 96; and the respirations 20. The blood pressure was 108 systolic and 74 diastolic.

Laboratory Studies. The hemoglobin was 10 grams per 100 ml. The white blood cell count was 6,500 per μl on admission, rising to 8,200 during hospitalization. Differential count revealed 61 per cent neutrophils and 39 per cent lymphocytes; repeat differential examination was unchanged. The urine contained 60 mg of albumin, and microscopic examination revealed 6 eryt' ocytes and 1 granular cast per high-power field. Kahn test was negative. Dark-field examination of serum for spiro-

chetes was negative. Cephalin-cholesterol flocculation test was 3 plus in 48 hours; thymol turbidity was 5 MacLaglan units. Total protein was 5.0 (albumin 2.4, globulin 2.6) grams per 100 ml. A thin blood smear for malarial parasites was negative. No pathogens were found on stool culture.

Course in Hospital. The patient's temperature ranged between 99° and 104°F, with the pulse varying between 78 and 90. Hematemesis occurred on the second hospital day and continued. He had several episodes of epistaxis. Hiccup began on the fourth hospital day and continued thereafter until death. Small, liquid, tarry stools bothered the patient and were associated with cramps. On the evening of the fourth hospital day he complained of sudden loss of vision, became rapidly dyspneic, had a short convulsion, and died.

DISCUSSION

Doctor Kretzschmar:* Features of these two cases that impress me are the similarity of signs and symptoms, and the acute, fulminating course of a febrile disease associated with jaundice in two young men, stationed in the tropics.

The past history of these two patients is not given but inasmuch as they had been on active duty as flight personnel, we can assume that both of our patients had been healthy men. Both had been on duty together. They had the same type of immunizations, including yellow fever. Both served in the same area where tropical diseases are known to occur. A third crew member was recovering from "infectious hepatitis."

The onset was sudden with malaise and vomiting, followed by a septic type of temperature associated with jaundice. The patients were acutely ill, toxic, and both had a palpable and tender liver. Mild splenomegaly was noted in one of them. The other had a tender abdomen. The vital signs given on the dates of admission are similar, *e. g.*, fever, relatively slow pulse rate (under 100), slightly labored respiration, and low blood pressure. The only apparent clinical difference was that the second case entered the hospital sooner in the course of his illness than the first one.

From the laboratory standpoint the only difference is that we are given more studies in one case than in the other. The white blood cell count was normal in both patients, the differential showing slight lymphocytosis.

The hospital course in the first case was marked by spiking temperatures with the pulse rate remaining below 100°F, hematemesis on the third day of illness, a white blood cell count rise to 15,000 with a shift to the left. On the seventh day of illness the patient's

*Lt. Comdr. Hanns Kretzschmar, MC, USN, Resident in Internal Medicine.

temperature dropped suddenly to 98°F, the pulse rose to 100, and subjectively he felt much better. He got out of bed, suddenly went into acute collapse, and died.

The hospital course in the second case was stormy, with the patient's temperature ranging between 99° and 104°F and the pulse remaining below 100. Hemorrhagic manifestations became evident in the third day of his illness in the form of hematemesis, epistaxis, and melena. The white blood cell count remained low; however, a left shift was noted. This patient died suddenly after loss of vision, a brief episode of dyspnea, and a short convulsion. One brief remark on the hiccups: persistent hiccuping occurred in both instances after the onset of gastric hemorrhage and its cause could be explained on the basis of gastric irritation.

Since the symptomatology in both cases was alike I shall assume a common cause. This tends to preclude diseases other than those due to poison or infection. From the standpoint of a possible toxic cause, a wide variety of chemical compounds, including dinitrobenzene, trinitrotoluene (TNT), picric acid, dinitrophenol, phosphoreted hydrogen, some of the anesthetics, phosphorus, and heavy metals, are well-known causes of acute yellow atrophy. A similar picture may arise after ingestion of the male fern and poisonous mushrooms.[1] During the past few years attention has been paid to a disease, mostly seen in Jamaica but also in India and Egypt, morphologically characterized by occlusion of the hepatic veins. This entity is referred to as "veno-occlusive disease of the liver." It is observed mainly in children but also among adults. All cases described occurred in poorer economic groups, where malnutrition or subnutrition may be present, yet it is believed that some toxic agent plays a major role in this disease. In all the published cases the patients habitually drank a variety of "bush tea." These are infusions of various herbs, seeds, and roots. Senecio (ragwort) poisoning may exhibit the same features as veno-occlusive disease. The course of this disease is either acute, subacute, or chronic. The acute form of veno-occlusive disease is characterized by the sudden development of abdominal pain, hepatomegaly, and ascites. Vomiting is common. Some of the patients rapidly develop liver failure and die.[2,3] It is quite unlikely that our pilots were malnourished or had partaken of "bush tea," yet some reported cases closely resemble the clinical picture that they presented.

This leads to the discussion of the infectious origin of the cases under consideration. One crew member was said to be recovering from infectious hepatitis; that could well be a clue. The incubation period of infectious hepatitis is normally given as between two and six weeks, and these patients could have been exposed to infectious hepatitis through contact with the third crew member. Lucke and Mallory,[4] in 1946, gave a thorough description of the fulminant form of epidemic hepatitis among members of the armed services stationed

all over the world. The incidence of occurrence of this form was as high in the Mediterranean area as elsewhere. Of the 196 fatal cases of epidemic hepatitis, 94 (53 per cent) died in less than ten days, most frequently between the fourth and ninth day. The clinical picture was characterized by a short and stormy course, either in the form of the "infectious type" with high temperatures, malaise, and general aching or a "gastrointestinal type" with anorexia, nausea, and epigastric discomfort predominating. Jaundice usually appeared by the second or third day. In nearly all cases the pulse rate was elevated when there was fever. The features tending to differentiate the diagnosis in the patients under discussion from acute fulminating hepatitis is, in my opinion, the different course of the disease in these cases. There are no real spiking temperatures and in fulminating hepatitis there is no "well day" as we were informed that the first case had. The mode of dying is quite different, patients with fulminating hepatitis usually going into a deep coma preceded by cerebral symptoms of a more gradual onset.

Inasmuch as both patients were stationed in tropical regions, *e. g.*, in Saudi Arabia, the East Coast of Africa, et cetera, any number of infectious diseases, occurring endemically, or at times in epidemics, must be considered. Let us confine our attention to those diseases that are associated with fever and jaundice. Dengue, Rift Valley fever, echinococcosis, and visceral leishmaniasis (kala-azar) are readily ruled out by their entirely different clinical course, which is mostly milder, more chronic in the case of dengue and dengue-like fevers, or usually associated with a skin rash in cases of leishmaniasis.

Acute amebic hepatitis develops during the acute stage of the intestinal infection or during remission. Generally there is a history of amebic infection. There is right upper quadrant pain with an enlarged and tender liver. The fever is high, and the white blood cell count usually ranges between 20,000 and 30,000 with a marked increase of the neutrophils. I think that the lack of information in the history in regard to intestinal parasites and the initial low white blood cell count are sufficient reasons to exclude the possibility of an amebic hepatitis.

The relative bradycardia, the initial absence of leukocytosis, and the severeness of the clinical picture made me think of typhoid fever. Formerly it was believed that typhoid fever seldom occurs in the tropics. It has been commonly confused with malaria, and in the southern part of the United States it was common to diagnose "typhomalarial fever."[5] The complications in typhoid fever include intestinal hemorrhages, intestinal perforation, pneumonia, meningitis, myocarditis, and sometimes terminal jaundice. Here again, however, a "well day" is not seen preterminally in cases of severe typhoid fever. In addition, these patients, being members of the armed services, certainly were immunized against typhoid making this diagnosis more unlikely.

The protocol mentions that the crew were exposed to rats, but adds that the urine and serum were negative for spirochetes by dark-field examination. Of the leptospiroses we have to consider Weil's disease and relapsing fever.[6] If we compare the picture of Weil's with the cases in point we find a few striking differences: Several of the cardinal features of Weil's disease are missing, namely the myalgias, the conjunctivitis, and the headache. Also in Weil's disease the onset of jaundice is on the fifth or sixth day of illness. The search for spirochetes by means of dark-field examination is not always successful but they may be found in the blood within the first five days of illness. A search of the urine would be futile, because positive results are not expected until the second week of illness. We find fewer differences when we consider relapsing fever. In the African tick fever a high white blood cell count is noted and the pulse rate is accelerated. I think we may dismiss these diseases.

Allow me to quote here the description of another disease, taken in part from Cecil's Textbook of Medicine: "Yellow fever is an acute viral disease characterized by sudden onset, prostration, moderately high fever, a pulse rate slow in relation to temperature and, when severe, by vomiting of altered blood, albuminuria and jaundice. It is endemic in the tropical rain forests of Africa and South America.... Fatal cases often exhibit hiccup, copious vomiting of altered blood, tarry stools and anuria.... Death occurs most frequently from the sixth to the ninth day."[7] Leukopenia is sometimes pronounced.

At first I thought that the protocol presented nothing more than a textbook description of yellow fever. However, there is one stumbling block: Both patients were inoculated against yellow fever. Vaccination against yellow fever is said to be very effective and antibody titers are known to persist for at least 6 years. One of the most conclusive evidences that vaccination is an effective procedure in protection against yellow fever is the fact that since introduction of yellow fever vaccine no accidental cases of the disease have occurred.[8] Therefore, the fact that the patients had been inoculated against yellow fever is strong evidence against that disease.

Up to this point, most of the diseases discussed were chosen under the assumption that the major pathologic condition was massive liver necrosis, or at least extensive heptocellular damage. Let us therefore examine the protocol critically and see whether we find indications justifying such an assumption. In the first case we are informed that the patient was jaundiced; however, no mention is made that the jaundice deepened, *e. g.*, that "liver cell destruction" was progressive. The same is true in the second case. The liver was palpable and tender in both cases, but no mention is made as to whether this liver enlargement was progressive or regressive. Liver enlargement is seen in many other conditions, quite often on the basis of congestion, and in acute congestion this enlargement is accompanied by pains in the liver area and tenderness of the liver to palpation.

The urine was positive for bile in the first case. This merely means that the patient's serum bilirubin was elevated. We know, however, that the direct bilirubin of serum has a much lower renal threshold than the indirect variety, therefore bilirubinuria is rare in the form of hemolytic icterus. In occasional cases, however, bilirubinuria is found if liver damage has taken place as a secondary result of anemia or hemolysis. That liver damage may have occurred is suggested in the second case by the abnormal cephalin flocculation and thymol turbidity findings. These tests are by no means diagnostic of severe hepatic destruction. I think that one is justified in considering the possibility that the jaundice may be on the basis of blood destruction rather than primary liver disease. Insofar as the hemoglobin is concerned we only have two bits of information: 13.5 grams of hemoglobin early in the disease of the first patient and 10 grams later in the course of illness in the second case. If one assumes that the patients were healthy prior to their illness and were ill for only two days before the examination, one wonders somewhat about the value of 13.5 grams of hemoglobin in a young male. There is definite evidence of reduction of the hemoglobin content in the second case, but whether on the basis of blood loss or on the increased hemolysis cannot be determined.

However, I think the question of blood destruction justifies the inclusion of malaria in the differential diagnosis.[9-11] The incidence of malaria is quite high in the tropics. The incubation period in vivax and falciparum infections are roughly the same, between 9 and 14 days. As far as the clinical picture is concerned there is such a great variety of different forms reported that a lengthy discussion of the problem may still not give a clear picture. Therefore I will discuss the possibility of malaria only on the basis of the information given in the protocol instead of trying to list all the possible clinical forms of malaria infection. The most probable is *Plasmodium falciparum*, the etiologic factor in malignant tertian malaria. The course of the disease may be short and violent, starting with a fever which persists in a spiking manner. Our first patient had a "good day" on the seventh day of his illness. I do not think that in any other disease which we have so far discussed, including fulminating hepatitis and yellow fever, the patient feels well and gets out of his bed on the same day he dies. Malaise and vomiting is a feature of many infectious diseases and is also prominent in malaria. Bradycardia occurs both in dengue and yellow fever, but here more as an absolute phenomenon, whereas our patients showed a relative bradycardia, the pulse rate remaining under 100.

The white blood cell count in our cases was normal on admission. The development of leukopenia is usually observed in yellow fever, dengue, and sandfly fever at the onset of the disease, while the count in malaria is usually about or below normal level. The neutrophils do not usually show a relative increase, as generally seen in bacterial

infections. In the former diseases mentioned one almost invariably finds a lymphocytosis.

In malaria, jaundice may occur on the second day, earlier than in yellow fever. In malaria the liver is usually palpable; the spleen, however, may or may not be felt in the acute stage. Splenomegaly is more a feature of the chronic forms of malaria. Furthermore, it depends on the type of plasmodial infection, being more pronounced in infections with *Plasmodium vivax,* but less with *Plasmodium falciparum.* Hepatic involvement is almost invariably present in malaria, which explains the discrepancy between visible jaundice and minimal evidence of hepatic disease; in other words, the jaundice is more on the basis of hemolysis than liver damage.

Both patients had signs of renal involvement. Albuminuria is commonly seen in high fever, but when accompanied by red blood cells and casts, the renal lesion is thought more serious. Malarial nephritis occurs in falciparum infection, but is less common in other malarial infection. Renal involvement is also noted in yellow fever and is most pronounced in Weil's disease.

No mention has been made of two symptoms: hiccups and hemorrhagic manisfestations. Both of these symptoms are pronounced in the course of yellow fever, and bleeding can occur in fulminating hepatitis, the mechanism probably being a disturbance in prothrombin production. Hemorrhagic tendencies also occur in malignant malaria, the mechanism here thought of being due to congestion of the capillaries. Hiccups, epistaxis, and blood in vomitus and stool are also features of malignant malaria.

Human malaria is an infection of the erythrocytes. When the trophozoite matures, the red blood cell is destroyed. Large numbers of infected erythrocytes are destroyed and phagocytized before maturation of the parasite. This results in a rapid loss of erythrocytes. Furthermore, Wong,[12] in 1945, proposed that there must be an unidentified factor present during a paroxysm, which inhibits full oxygenation of the blood hemoglobin. Destruction of large numbers of red blood cells releases parasites, pigment, and erythrocytic debris. This throws a tremendous burden on the phagocytic cells of the body, mainly cells of the reticuloendothelial system, which show generalized swelling. The blood flow through the capillaries is slowed, sometimes to the point of stasis. The question of whether or not there is true "plugging" of the capillaries is not yet solved. For unexplained reasons these changes have a predilection for the capillaries of the brain. They also are more frequently found in organs or systems to which the most prominent clinical features were referrable. I think it conceivable to explain the hemorrhagic features of our patients on the basis of congestion in the gastrointestinal tract. On the same basis one also can explain the hiccups.

It is difficult to explain the mode of death in both cases unless one assumes that on the basis of the pathophysiology of malaria,

anoxia and acute capillary congestion of the vessels of the brain and the heart were the final events.

On the basis of clinical manifestations, three types of malignant malaria have been described: (1) cerebral manifestation (hyperpyrexia, coma), (2) algid manifestation (diarrhea, fever), and (3) bilious remittent fever. It also is emphasized that mixed forms can occur.

My clinical diagnosis is pernicious or malignant malaria, due to *Plasmodium falciparum*, most likely of the bilious remittent fever type. I admit, however, that it is difficult to explain why these two airmen simultaneously developed such a fulminating form of malarial infection and in any type of infectious disease, the final diagnosis comes, in most instances, from the laboratory.

Doctor Sise:* There is very little left to say. I will, however, differ about everyone being vaccinated as they should in the armed services. Certainly there were a number of individuals who missed vaccination for smallpox during World War II and the Korean Conflict. The clinical phase of both these cases is so clearly associated with yellow fever that I would not be surprised if this were the diagnosis. We know that this was an endemic area. Onset was rapid with high fever, low blood pressure, vomiting of coffee-ground material, hiccups, sudden and what seemed, unexplained death. When patients appear ill from yellow fever in the first stage, which was the case in both these individuals, a fall of temperatures in the middle of the course is usually not uncommon and may be an unsettling event. A return of fever with shock and sudden death is consistent with yellow fever.

Being in cardiology I was interested in the sudden death and low blood pressure which were consistent with myocarditis. As far as fulminating hepatitis is concerned, and as Doctor Kretzschmar has pointed out, early deaths are very similar to acute yellow atrophy and the patients die in a state of coma. Serum hepatitis is not associated with fulminating fever and would be less likely. An embolus as the immediate cause of death does not appear to be consistent. As far as falciparum malaria is concerned, that I have seen; acute yellow fever, I have not.

Falciparum malaria is an acute disease, but as far as we know the sudden and quick deaths are in those who have cerebral malaria. Doctor Kretzschmar brought out the possibility of Weil's disease with the characteristic signs of renal involvement, chills, and fever. The chills appear after a return of fever and manifestations of bloody diarrhea or uremia.

With this type of picture, I believe that these individuals missed or avoided yellow fever vaccination. I do not think they had falciparum malaria, but rather yellow fever.

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*Herbert S. Sise, M. D., Consultant in Medicine.

Doctor MacGregor:* I thought of using the reverse approach to these cases and first made up a differential diagnosis, then went through the list to see which were the most typical. Granting that there were four entities which should be considered, namely, Weil's disease, infectious hepatitis, fulminating malaria, and yellow fever, I chose yellow fever largely on the basis of epidemiology and because it seemed to fit the clinical factors that are known to us.

Yellow fever explains the course of two similar cases and a possible third that occurred at about the same time in personnel who had been similarly exposed. These points seem to me to be against the other three entities. I think that the probability of two people being exposed to rats and being infected is less likely. In the same way, having two cases of fulminating hepatitis at the same time is most unlikely. I think that many aspects of these cases, including the diarrhea, hematuria, convulsions, and death, were consistent with yellow fever, and that such a diagnosis is indicated.

Doctor Delabarre, Jr.:* I have never seen a case of yellow fever or Weil's disease but think it would be most unlikely that both patients would come down with the same type of malaria, with the same termination. I think yellow fever is the most likely diagnosis. Vaccination for yellow fever is not 100 per cent effective and we do not know when they were vaccinated.

Dr. Kretzschmar's diagnosis:

Cases 1 and 2. Pernicious or malignant malaria, due to *Plasmodium falciparum*, most likely of the bilious remittent fever type

Diagnosis of Drs. Sise, MacGregor, and Delabarre:

Cases 1 and 2. Yellow fever

PATHOLOGIC FINDINGS

Doctor McMahon: The spleen in case 1 weighed 700 grams and in case 2, 750 grams. The livers weighed 2,125 and 2,500 grams, respectively; the kidneys, 575 and 650 grams; and the hearts, 500 and 550 grams. The spleens were tense, with a thin capsule that tore easily. The pulp was soft, friable, and devoid of recognizable architecture. The livers were yellow-green to gray, congested, and firm. The architecture showed an interlacing group of swollen gray cords with irregular dark-green, pin-point dots throwing the gray cords into relief. Both hearts were enlarged and markedly dilated; the auricular walls were parchmentlike in thinness. The myocardium was soft, friable, and granular. The lungs were heavy and wet. The kidneys on section showed a swollen bulging cortex that was sharply demarcated from the congested medulla.

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Microscopically, the spleen showed marked congestion with washing out of the cells in the pulp. There were many macrophages filled with pigment. Some of the follicles were hyperplastic, but others tended to be replaced by larger, variable-sized cells with hyperchromatic nuclei (fig. 1). The liver showed empty sinusoids lined by numerous, large Kupffer cells filled with pigment (figs. 2 and 3). The capillaries of the heart and intestines were filled with parasitized erythrocytes and pigment debris. (figs. 4 and 5). The kidneys showed degeneration of the tubular epithelium.

Pathologic diagnosis:
Acute, fulminating malaria

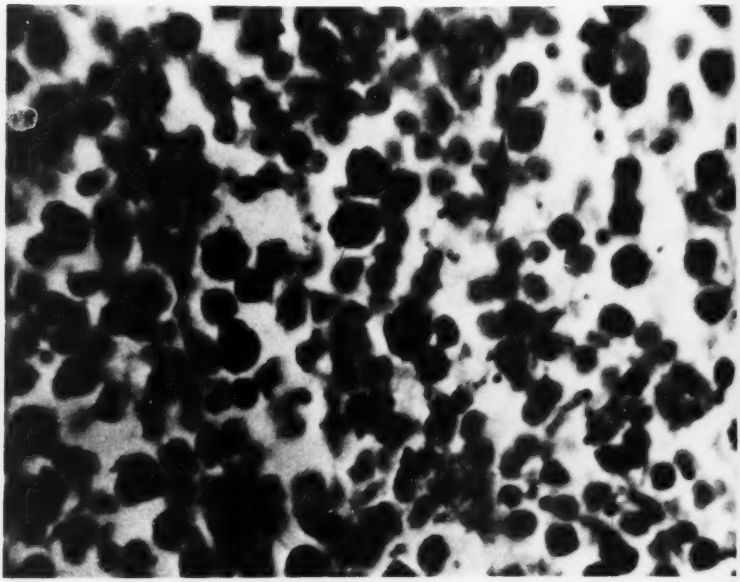

Figure 1. Spleen: Large atypical mononuclear cells and pigment debris, free and in macrophages. (× 430)

Even though we were in a so-called malarial belt and had dealt with transients from all over the Mediterranean area, the Near East, and Africa, we had not seen a case of malaria in the previous five years. Because of this we have not been malaria conscious. The clinical course of the disease in these two men certainly did not show the typical distinctive paroxysms with the cold, hot, and sweating stages. There are many sets of circumstances that could pave the way for the pernicious form, among which are alcoholism, excessive fatigue, high external temperatures, and a continuation of customary activity. It was postulated that these man, who flew their plane on a rather

heavy schedule, probably were fatigued, yet continued their activities even when indisposed.

Pernicious manifestations fall into three general groups; namely, the cerebral, algid, and gastrointestinal, plus a miscellaneous grouping. It was not easy to separate these cases into the various subdivisions of pernicious malaria and to say that they were purely algid, cerebral, gastrointestinal, or that they developed black-water fever. Some symptoms would suggest the gastrointestinal phase. Black vomitus occurred in both cases, and tarry diarrhea occurred in case 2. In this case many pigment granules and parasites were seen in the mucosal capil-

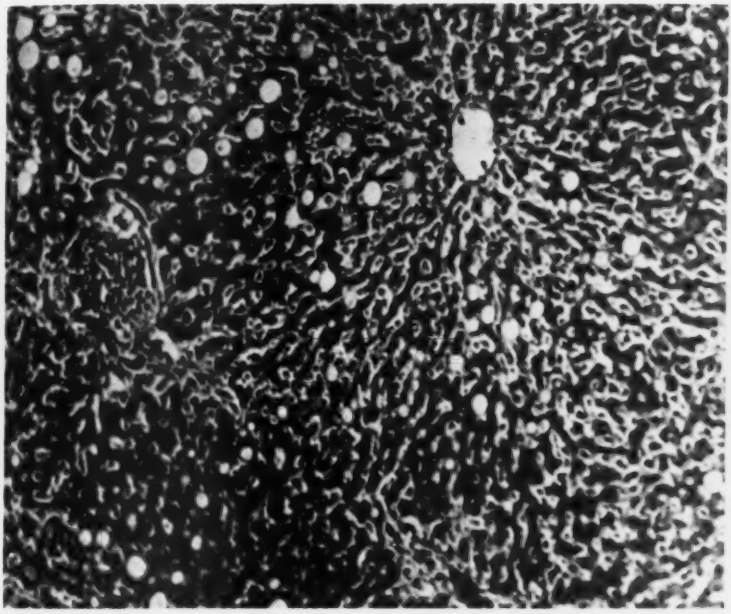

Figure 2. Liver: Low-power view showing empty sinusoids containing large Kupffer cells. (× 120)

laries of the gastrointestinal tract (fig. 5). The clinical history of delirium, agitation, loss of vision, and convulsions noted in case 2 was very suggestive of cerebral malaria. The pathologic findings of greatly enlarged spleen, kidneys, and liver, larger than those usually seen in acute falciparum malaria, together with the microscopic findings of early hemoglobinuric nephrosis suggested the diagnosis of black-water fever, but the complete clinical and microscopic picture of black-water fever does not seem to be proved by the clinical course and the autopsy findings. The myocarditis and pulmonary edema in case 1 with the terminal episode of shock and dyspnea suggested that death was a result of cardiorespiratory failure.

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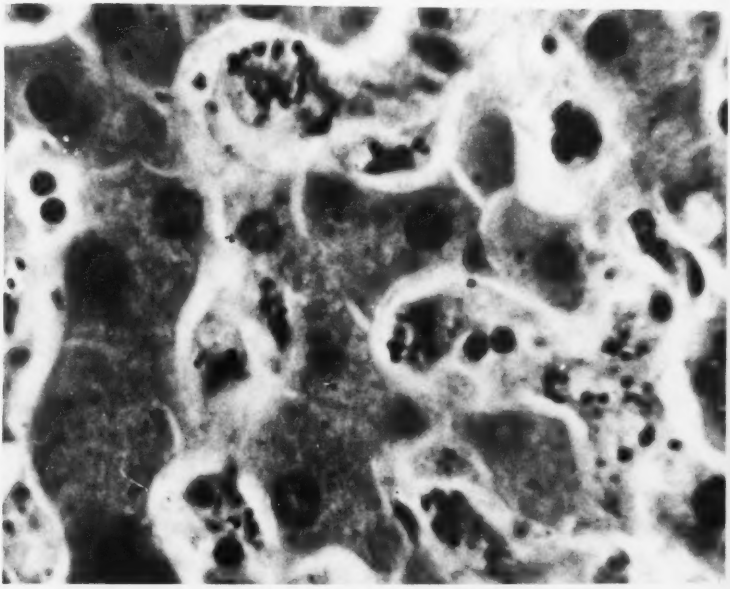

Figure 3. Liver: Sinusoids showing Kupffer cells filling sinusoids and stuffed with pigment and parasites. (× 430)

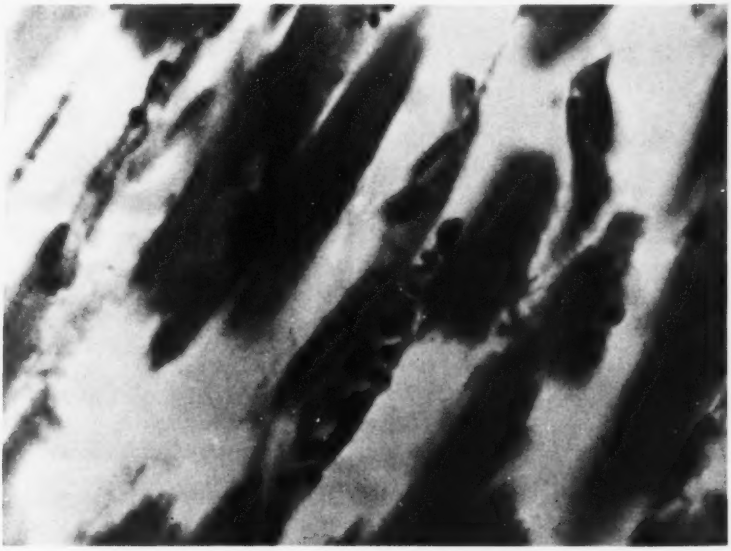

Figure 4. Heart: Capillary filled with parasitized erythrocytes. (× 430)

The epidemiology of their disease, if it was *Plasmodium falciparum* malaria, is interesting. These men were operating in areas where malaria is highly endemic and, in the past, epidemic. Central Arabia is notorious for oasis fever. In times past malaria has been epidemic in Aden. In conversations with the British Commandant, it was learned that several cases of malaria have been reported there in the past few years. The men stated that they were bitten by mosquitoes while staying in Asmara. It was unlikely that malaria was contracted in Asmara unless they brought the malaria-bearing mosquitoes with them.

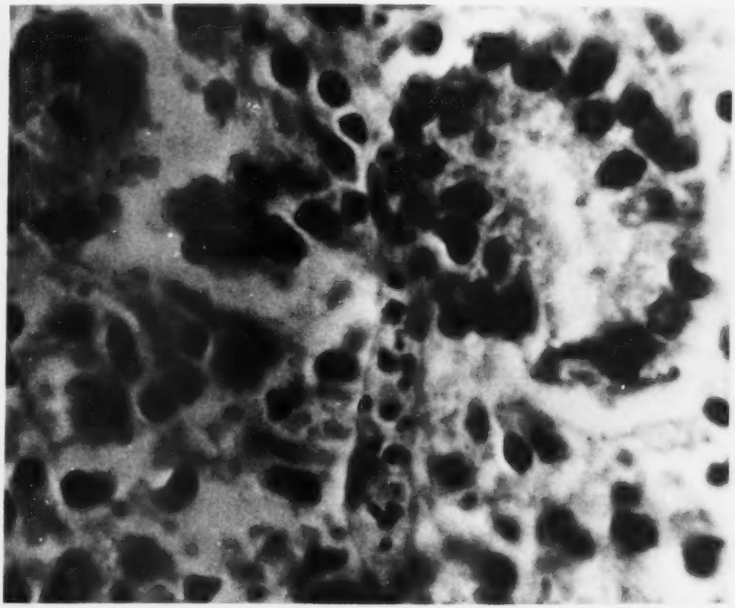

Figure 5. Small intestine (jejunum): Capillary showing pigment debris and parasitized erythrocytes. (× 430)

Asmara is located 7,000 feet above sea level, and Italian surgeons who operated in this area during the last war said they were of the firm conviction that no malaria was present in the high plateau in Eritrea. That leaves Massaua in Eritrea, which is at sea level and is known to be malarious. If this was the first acute attack, and from the clinical symptoms and the pathologic findings it seems to have been, then the mean incubation period of about 13 days would fit well with their stay in Massaua, Eritrea.

In conclusion it is well to bear in mind that although great strides have been made in the control of malaria, it is still a common disease in many parts of the world. In days of fast travel, when many military personnel and tourists pass through or visit endemic areas, this dis-

ease continues as a problem. In a recent communication from the Armed Forces Institute of Pathology concerning these cases, one of the staff made the following comment, which may be of particular interest to clinicians: "To my knowledge these two cases will make a total of four cases of fulminant malaria recorded here within the past four years, in which malaria was not diagnosed ante mortem. In one more case, the diagnosis was made when the patient was moribund." James is quoted in *Malariology* as follows: "It is characteristic of many pernicious symptoms that they tend to prevent the prompt diagnosis of the disease. They may do so either by presenting in a prominent manner a symptom which strongly suggests some other condition than malaria, or by presenting in a patient who is obviously very ill, an almost complete absence of what are known to be the usual clinical signs of malaria."[13]

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EPIDEMIOLOGIC STUDY OF TUBERCULOSIS IN THE U. S. NAVY AND MARINE CORPS

I. Methodology and Individual Factors

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PHILIP E. SARTWELL, *M. D.*

THE problem of controlling tuberculosis in the Armed Forces is still of considerable importance to the nation, despite the fact that in the U. S. Navy, as an example, the incidence of the disease has dropped from 6.8 per thousand per annum in 1903 to 0.8 in 1954.[1,2] It has been variously estimated that each case of tuberculosis in the Armed Forces costs the government about $60,000, when cost of training, hospitalization, and disability benefits are considered.[3] In the Navy in 1953 there were 742 persons diagnosed for the first time as suffering from tuberculosis who were adjudged as having contracted the disease while in service.[4] The government assumed responsibility for the care and disability benefits accorded these persons. The ultimate cost, then, of tuberculosis in the Navy for the year 1953 might be estimated as amounting to some $44,520,000.

In view of the continuing importance of tuberculosis in the Armed Forces and the nation, it is evident that a more complete knowledge of the epidemiology of the disease as it occurs in one or more branches of the Armed Forces should be of assistance to those charged with the protection of the health of service members.

Purpose

The primary purpose of this study was to attempt to determine what factors, such as personal attributes, environment, and particularly characteristics of service life, have been associated with excessive risk of development of tuberculosis in the U. S. Navy and Marine Corps. A secondary purpose was to aid in the evaluation of procedures designed to screen out tuberculous

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recruits prior to entry into the service and to find those cases of tuberculosis which might develop in service personnel after enlistment. Other branches of the Armed Forces may find the data in this study helpful in deciding whether they should adopt certain tuberculosis control procedures now practiced only by the Navy. These procedures are, specifically, the routine tuberculin testing of all recruits and the provision of annual x-ray examinations of the chest for all enlisted as well as officer personnel.

Previous Studies

For many decades there has been interest in the influence of environment and host factors in the epidemiology of tuberculosis in military, industrial, and institutional populations as well as in civilian populations. A limited review of the literature of the past 20 years on the subject reveals at least 74 articles dealing with the epidemiology of tuberculosis in various military forces in Europe and the Americas. An observation common to most of these studies is that military service, particularly during times of war, exerts an unfavorable influence on the incidence of tuberculosis in young adult males.

The Medical Department of the U. S. Navy has carried out studies on tuberculosis over the past 20 years or more; the work of Britten, Charter, and co-workers[5-9] is particularly noteworthy. Most studies, however, have dealt with mass data extracted from routine summaries noted on punch cards or taken from group statistical records. These studies have been descriptive of the distribution of tuberculosis within the services by such factors as age, sex, race, rank, length of service, severity of disease and, occasionally, by occupation. Satisfactory epidemiologic analysis of these data has been troublesome since the numbers at risk in each category frequently have not been determined. Again, in past studies, the term tuberculosis has often been rather inclusive; cases of pulmonary infiltration of unknown etiology have been included.

Two recent studies are particularly pertinent to this topic. The first, by Long and Jablon,[10] is a study of tuberculosis in the U. S. Army in World War II. The main purposes were to determine the efficacy of x-ray screening methods employed at induction and to delineate epidemiologic factors related to the occurrence of the disease in service. This study utilized the case-control approach. The other, by Palmer and associates,[11] investigated the subsequent incidence of tuberculosis in naval personnel who had been through a naval training center where their tuberculin status was determined. It was concerned especially with this factor and with the influence of body build on susceptibility. The approaches and findings of these two studies were known to the authors and were most helpful in our

investigation; they will be further discussed at a later point. Incidentally, a few of the tuberculosis cases analyzed in this report are presumed to have entered in Palmer's analysis as well.

METHOD OF STUDY

Choice of Study Group and Method of Analysis

Since 1949, the Navy has routinely tuberculin tested all new recruits; thus, this service affords an unusual opportunity to study a large population, uninfected on entry into the service. Other advantages, shared by the other armed services, are the availability of uniform personnel records providing information on service conditions and types of duty, and of detailed medical records with considerable uniformity of diagnostic standards, nomenclature, and procedures. It was therefore decided to analyze the Navy material.

Three general methods of epidemiologic study were theoretically possible. The first was to relate the cases of tuberculosis to the service population out of which they arose. This was impossible because for many of the factors which it was desired to study, the number of naval personnel at risk was not known and could not be determined from service personnel records. The second was to follow up individuals after ascertaining their status with respect to each characteristic and in this way to determine differential incidence rates. This method was possible and would have given the most reliable information, but would necessitate an expenditure of time, effort, and funds beyond the available resources. The third approach, which was necessarily adopted, was the comparison of a series of cases with a suitable series of controls.

A number of workers have pointed out the uncertainties of selection involved in study of groups of people hospitalized for a disease, and some have even denied the validity of such an approach. It should be pointed out that these objections have much less force where one is dealing with a hospital system, and can be confident that nearly all recognized illnesses occurring in members of the community (in this case a military service) will be hospitalized within the service and recorded as cases in the service-wide record system.

The Study Group

Cases of tuberculosis diagnosed in 1953 and 1954 were chosen for study because case records of this recent period were generally complete and available, and because foreign service and combat experience during the Korean Conflict could be considered. Both cases who were tuberculin positive and tuberculin negative on entry were included, though many of the analyses pertain only to the originally tuberculin-negative group. Practi-

cally all included cases entered the service in 1949, the year when service-wide tuberculin testing of Navy recruits was adopted, or subsequently.

Some cases of tuberculosis developing in 1953-1954 were probably omitted from the study for such reasons as failure to detect lesions on roentgenograms, omission of roentgenograms, or erroneous diagnoses.

The diagnosis, "pulmonary infiltration of unknown etiology" (Code 0070 of the Joint Armed Forces Statistical Classification and Basic Diagnostic Nomenclature (BDN, 1949) is frequently employed by the Navy for cases where the clinical and roentgenologic findings are not considered sufficiently characteristic to warrant a specific diagnosis of tuberculosis. In official reports these cases are sometimes classified under tuberculosis. No person with this diagnosis was included in the study because it was believed that only well-supported cases should be included. On the other hand, proof of diagnosis by recovery of *Mycobacterium tuberculosis* was not required because of the very thorough and careful diagnostic study of all cases in the service and the belief that the number of tuberculosis cases that would be erroneously excluded by such a requirement would exceed the number of erroneously included cases if demonstration of the organism was not a criterion of acceptance. Table 1 shows that *Myco. tuberculosis* was recovered from 296 (73 per cent) of 405 persons in the study group and that there was not a significant

TABLE 1. *Demonstration of* Mycobacterium tuberculosis *at final diagnosis in relation to tuberculin sensitivity on first entry into service—all personnel*

Demonstration of *Myco. tuberculosis*	Study group Tuberculin reaction on entry into service									
	Negative		Doubtful		Positive		Unknown		Total	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Yes	171	73.0	6	75.0	66	80.5	53	73.0	296	74.6
No*	63	27.0	2	25.0	16	19.5	20	27.0	101	25.4
Subtotal	234	100.0	8	100.0	82	100.0	73	100.0	397	100.0
Records missing**	2		0		4		2		8	
Total	236		8		86		75		405	

*Records show definite search for organism with negative result.
**Information as to bacteriologic status missing.

difference in this regard between those who were tuberculin positive, tuberculin negative, or untested on entry into the service.

Thus, it is to be expected that a very small number of persons erroneously diagnosed as having tuberculosis were included, and a somewhat larger number who did have tuberculosis were excluded from the study. The probable effect of the first error is to reduce a little the size of any true differences between the study group and the controls; the latter error should have no effect unless the erroneously excluded cases have characteristics different from those of the positively diagnosed cases.

In résumé, the group termed the study group of tuberculosis cases consists of all those individuals who were first diagnosed as having tuberculosis while in the Navy or Marine Corps in 1953 or 1954, and whose first entry into service occurred in 1949 or later. All cases with a final diagnosis of any form of tuberculosis are considered. Those individuals known to have been tuberculin negative on entry into the service will be referred to as the basic study group. Many of the analyses will be limited to enlisted men of the Navy and Marine Corps, because they comprise nearly all the cases.

In many of the tables, data pertaining to all individuals, regardless of tuberculin sensitivity at induction, and data pertaining only to those who were tuberculin negative at induction, are both presented. Where this is done, the line designated "A" refers to the whole group and line "B" below, to the "basic study group" of nonreactors.

It will be noted in table 2 that case records were not received on 70 of the recorded cases of tuberculosis. To determine if there were any major characteristics of this absent group which might bias, by their absence, the attributes of the group actually received and studied, especially in relation to the control, the official Navy summary case cards of the 70 were tabulated. The "not received" group differed significantly in several respects from the study group. It must be borne in mind, however, that at least 10 or 11 of the 70 cases would have been rejected for study had they all been received, assuming that the 15 per cent over-all rejection rate found to apply to the records received were to apply to them also. The principal reason for rejection of received records was service prior to 1949; hence a rejection of much more than 15 per cent of the group whose records were not received could be expected if this group included a high proportion of older men with longer service, as was found to be the case.

The proportion of enlisted male Navy medical and dental technicians was high in the "nonreceived" group; the inclusion of

all these cases would, however, only raise the percentage of this occupational category in the study group from 5.1 per cent to 6.6 per cent. The nonreceived group also included a higher proportion of minimal cases (31 per cent as compared with 21 per cent) and a corresponding deficiency in far-advanced cases. However, if all of these nonreceived case records were received and accepted, the percentage of far-advanced cases in the total study group would fall only 1.4 per cent. Nevertheless, these differences must be kept in mind in subsequent discussion of these variables.

TABLE 2. *Derivation of study group of cases of tuberculosis, U. S. Navy and Marine Corps, 1953-1954*

Category	Year 1953	Year 1954	Total
Cases of tuberculosis recorded in official U. S. Navy reports	911	754	1665
Cases not included in study*	696	564	1260
Duplicates and cases known prior to year stated	(85)	(35)	(120)
Tuberculosis existed prior to service	(84)	(79)	(163)
Persons diagnosed "pulmonary infiltration of unknown etiology"	(252)	(227)	(479)
Persons with service prior to 1949**	(261)	(167)	(428)
Case records not received	(14)	(56)	(70)
Remainder: Final study group	215	190	405

*Nearly all screening was done on Navy FP Summary Cards prior to request for detailed individual records. However, 73 (15 per cent) of the 478 individual records actually received were rejected after receipt because of service prior to 1949.

**Five persons known to be tuberculin negative on entry into the service in 1948 were retained in the study.

The Control Group

It was considered that the only control group which would yield the desired information and at the same time could practicably be employed would be a series of cases of some other disease. Such a control group offers several advantages; it can readily be chosen on the same basis, with respect to time factors, as the study group, and the medical records for major illnesses provide the information needed for the purposes of the study. The one serious disadvantage lies in the fact that every illness or accident involves some selection, such that the group cannot be regarded as entirely representative of naval personnel in general. In other words, instead of the desired comparison, the epidemiology of tuberculosis would be contrasted with that of another condition. A number of conditions and diseases such as accidents, upper respiratory disease, venereal disease, mental

disorders, allergic conditions, and dental conditions were considered and rejected because they were known or presumed to be selective in one way or another. Acute appendicitis was the condition which seemed to come closest to satisfying the requirements for a control illness. In order to study its distribution, a random sample of 20 per cent of all cases of appendicitis in the Navy and Marine Corps in the years 1953 and 1954 was compared with the composition of the services for the same years for those characteristics the distribution of which, in the service, could be obtained. This study showed that the appendicitis cases had a small but significant deficit of officers and of Negro personnel, and were younger on the whole than service personnel in general. This age difference is revealed by estimating attack rates per 1,000 population per year from the sample. The rates go down with increasing age in each year from 7 per 1,000 per year for personnel under 20 to 1.5 for personnel over 35. This would account for the deficiency of officers in the appendicitis sample.

There are also differences in length of service. These, however, are at least partly fictitious because inactive-duty periods were counted in total service in the Bureau of Personnel records utilized for getting the composition of the entire Navy and Marine Corps, but not in the medical records from which the appendicitis data were taken.

While the agreement was not as good as might be hoped, further comparisons which were made between the appendicitis control series finally chosen and the Navy and Marine Corps as a whole, which will be presented later, provide a more encouraging picture. These comparisons are with respect to reserve status, rank, service occupation, tuberculin sensitivity, and height and weight. We need not be seriously disturbed by the differences in age, because the selection for time of enlistment and of diagnosis imposed in the study nearly eliminated age differences; nor by the differences in length of service because the control series was matched for length of service with the tuberculosis cases.

The control group chosen consists of individuals first diagnosed as having acute appendicitis (BDN 5500-5505) in the Navy or Marine Corps in 1953 or 1954, whose first entry into service occurred in 1949 or later. It was estimated that a 20 per cent random sample of all appendicitis cases would yield a sufficient number of records from which to derive a control sample. This was secured by drawing the records of all appendicitis cases with serial numbers ending in either "6" or "7". Because a number of variables to be studied, such as place and length of foreign duty, ship service and Korean experience, depended on a close similarity between study and control groups with respect to length of service prior to illness, it was decided to

match the control to the study group for this factor, using Navy FP Summary cards. This was done by discarding, by a random method, sufficient cards from the control series in those length-of-service subgroups that were overrepresented to make the two series (cases and controls) proportional. Subsequent nonreceipt of some detailed individual records and rejection of others disturbed the agreement as to length of service somewhat but not seriously. Table 3 indicates the selective procedures employed.

TABLE 3. *Derivation of control group of cases of acute appendicitis*

Category	1953	1954	Total
Cases of acute appendicitis, official U. S. Navy reports	4824	4073	8897
Approximately 20 per cent random sample* furnished by Navy	987	791	1778
Matched and subgrouped by length of service with enlisted tuberculosis group, using Navy FP cards, then subgroups reduced at random** to approximate size of comparable enlisted study subgroups. Screened for duplicates and errors.			
Remainder:	288	250	538
Cases rejected because of service prior to 1949	(23)	(10)	(33)
Case records not received	(7)	(15)	(22)
Remainder: Final control group	258	225	483

*By selection of service serial numbers ending in either "6" or "7".
**By using various numbers of next-to-last digit in serial numbers to obtain desired percentages.

The final control group, like the tuberculosis case series, consisted almost entirely of male enlisted Navy and Marine Corps personnel. Many of the comparisons are, therefore, necessarily limited to enlisted men.

The Records Used

The records employed were the individual health record, known as the "health record" or "medical jacket," and the clinical records of hospitalization.

The individual health record, which is maintained on every member of the Navy and Marine Corps, contains a copy of the induction medical history and physical examination, induction x-ray records (but rarely the film itself), immunization record, a running record and summary of all out-patient and hospital examinations and treatment, a venereal disease record, an abstract of service and, in the case of tuberculous individuals in particular, many personnel documents pertaining to action of clinical and physical evaluation boards. In the case of tubercu-

lous personnel, the health records were usually on file at the Navy Medical Record Center at Garden City, Long Island, N. Y., because nearly all of these individuals had left the service for Veterans Administration facilities or elsewhere.

Procurement of the individual health records of the control group was a difficult matter. A large percentage of the individuals concerned were still in service in 1955 and obtaining their basic health records necessitated official requests to ships and stations all over the world. Officer records, in particular, were most difficult to procure. The individual health records of appendicitis cases who were still in the service were at their duty stations; those of discharged personnel were at Garden City or in Navy files in Washington.

The clinical records of hospitalization were usually obtained from the hospital concerned; otherwise from Garden City or from the Veterans Administration, where they were often on loan. Complicating their procurement was the fact that many tuberculosis service personnel had passed through as many as four service hospitals throughout the world prior to final in-service study of nearly all cases at the two naval tuberculosis centers—U. S. Naval Hospital, St. Albans, Long Island, N. Y., and U. S. Naval Hospital, San Diego, Calif. All tuberculosis case records had been finally reviewed in the Bureau of Medicine and Surgery, Department of the Navy. In many instances, individuals who had suffered from appendicitis were treated by appendectomy aboard ship or in a small infirmary, and the records were often less detailed than those of the tuberculosis cases. This fact is reflected in the higher percentage of "unknowns" seen throughout the tables in reference to the control group when compared to the study group.

Where pertinent portions (forms) of records and expected notations on received and included forms were missing and unobtainable, the lacking information has usually been included under "unknown" in the tables for simplicity. Of the expected usable tuberculosis case records, 87 per cent were received, and of the control records, 95 per cent.

FINDINGS

Sex and Race

Table 4 gives the distribution of subjects by sex, rank, and service. The racial distribution is shown in table 5.

Only eight female personnel in category A are represented in the study and control groups combined. This number is too small to permit any inference being drawn. However, it is of interest that although female personnel are not proportionately

assigned to sea duty or foreign service there were seven females among the cases and only one among the controls.

TABLE 4. *Composition of study and control groups, by sex, rank, and service*

Category		Cases		Controls	
		Male	Female	Male	Female
Navy					
Officer	A	5	1	0	0
	B	2	0	0	0
Enlisted	A	314	4	366	1
	B	185	0	253	1
Marines					
Officer	A	3	0	0	0
	B	1	0	0	0
Enlisted	A	76	2	116	0
	B	46	2	78	0
Total	A	398	7	482	1
	B	234	2	331	1

"A" refers to the group, regardless of tuberculin sensitivity.
"B" refers to tuberculin-negative individuals.

TABLE 5. *Male enlisted personnel in study and control groups, by race*

Race		Study		Controls	
		Number	Per cent	Number	Per cent
Caucasian	A	351	90.2	469	97.5
	B	211	91.3	324	97.9
Negro	A	25	6.4	8	1.7
	B	14	6.1	4	1.2*
All others	A	13	3.4	4	0.8
	B	6	2.5	3	0.9
Subtotal	A	389	100.0	481	100.0
	B	231	100.0	331	100.0
Unknown	A	1		1	
	B	0		0	
Total	A	390		482	
	B	231		331	

"A" refers to the group, regardless of tuberculin sensitivity.
"B" refers to tuberculin-negative individuals.
*See text.

Of the controls, 1.7 per cent were Negroes; of the tuberculin-negative controls, 1.2 per cent (table 5). However, 3.9 per cent of the entire personnel of the Navy and Marine Corps in 1953 were Negroes,[4] and probably nearly all persons of this race were enlisted men; data were not available for 1954. This discrepancy makes for uncertainty as to whether the control cases of appendicitis reflect the composition of the service with respect to race. In any case, even if one accepts 3.9 per cent as the true figure, it is still significantly lower than the percentage among the cases (6.4 per cent) and, of course, the observed percentages are markedly different. There was also an excess of "other races" among the cases, but the numbers for any single racial group are too small to be meaningful.

Religious affiliations were examined because of the possibility that they might reflect ethnic differences in susceptibility; it has been suggested that Jews have lower susceptibility to tuberculosis. No significant differences were observed between cases and controls in the percentages who were of each faith, but only six persons of Jewish faith were in the study.

Age at Entry Into Service and at Final Diagnosis

The age distribution of both groups was examined. As was expected, the distribution of ages at entry in the basic study group and in controls was almost identical, because the control group was matched by length of service to the study group and all men had less than 6 years of service. Relatively few enlisted men enter the Navy after age 21. The ages at final diagnosis differed slightly.

Information in the medical records on the level of civilian education prior to service was insufficient to permit this to be studied.

Tuberculin Sensitivity

The tuberculin reaction at entry into service was of particular importance. There were 75 cases and 115 controls for whom this was unknown.

Tuberculin testing of recruits in the Navy and Marine Corps has been done since 1949 at all basic training centers of these services. The standard test dose employed throughout has been 0.0001 mg of PPD. Injections are given and reactions are read after 72 hours (in no case earlier than 48 hours) by skilled medical technicians under the supervision of medical officers. Since the beginning of the program in 1949 the degree of reaction has been recorded in conformance with the standards of the National Tuberculosis Association as follows:

Negative – No induration.
Doubtful – Trace of induration of 5 mm diameter or less.
1 plus – Induration of more than 5 mm, not exceeding 10 mm.
2 plus – Induration of 10-20 mm diameter.
3 plus – Induration over 20 mm in diameter and marked erythema.
4 plus – Severe induration and an area of necrosis.

While visiting the U. S. Naval Training Center, San Diego, Calif., in February 1956, the testing and recording of recruits was observed, and the processing was found to be technically and administratively excellent. In addition, it was noted that all recruits showing doubtful or positive reaction, or having a history of contact with a tuberculous person, were given a 14- by 17-inch x-ray film examination, in addition to the routine 70-mm film taken on all recruits at the station.

The composition of our case and control series with respect to tuberculin sensitivity is presented in table 6 and in figure 1.

TABLE 6. *Tuberculin sensitivity on first entry into service, all personnel*

Reaction	Cases		Controls	
	Number	Per cent	Number	Per cent
Type of reaction				
Negative	236	71.5	332	90.2
Doubtful	8	2.4	3	0.8
Positive	86	26.1*	33	9.0*
Subtotal: Injected and read	330	100.0	368	100.0
Unknown	75		115	
Total	405		483	
Distribution of positive and doubtful reactors				
Doubtful	8	8.5	3	8.3
1 plus	29	30.8	16	44.4
2 plus	27	28.7	10	27.8
3 plus	24	25.5	4	11.1
4 plus	6	6.4	3	8.3
Total	94	100.0	36	100.0
Type of reaction of all enlisted personnel with negative chest x-ray findings on entry into service				
Negative	225	73.7	330	91.0
Positive or doubtful	80	26.3*	33	9.1*
Subtotal	305	100.0	363	100.0
Unknown	61		103	
Total	366		466	

*P <0.001

The representativeness of the controls can be judged by comparison with Navy-wide experience. The data in table 7 show the percentages of positive and doubtful reactors among recruits

in the entire Navy and Marine Corps in the years 1949 to 1954. These figures were kindly supplied by Captain John F. Chace, MC, USN. Applying each of these figures to the number of male

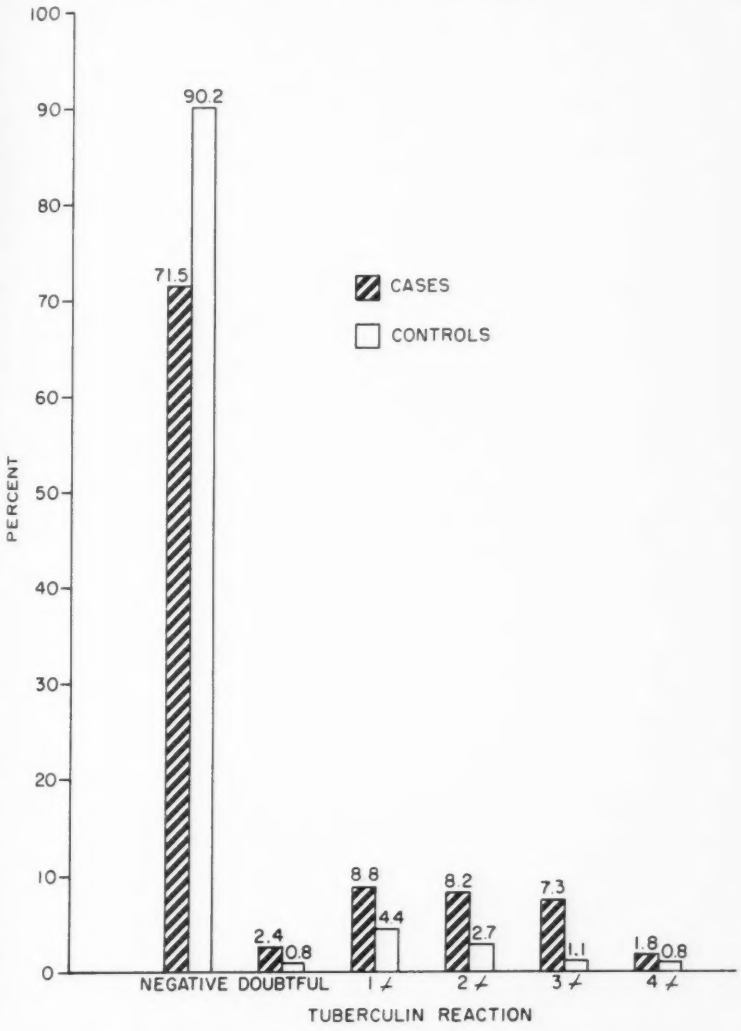

Figure 1. Tuberculin sensitivity on first entry into service, all personnel.

enlisted controls who entered the service in the corresponding year, the expected number of reactors for that year and, by addition, for the entire 6-year period, can be estimated. As table 8

shows, 36 controls were actually positive or doubtful reactors, while 41 would be expected. This agreement is considered fairly satisfactory.

TABLE 7. *Induction tuberculin reactions, U. S. Navy and Marine Corps recruits, 1949-1954*

Year	Positive (per cent)	Doubtful (per cent)	Total doubtful and positive (per cent)
1949	8.6	0.7	9.3
1950	11.1	0.7	11.8
1951	10.2	2.4	12.6
1952	10.0	2.4	12.4
1953	5.1	0.7	5.8
1954	4.5	0.8	5.3
Average (1949-1954)	8.8	1.7	10.5

TABLE 8. *Observed and expected induction tuberculin reactions, male enlisted control group, 1949-1954*

Year	Tuberculin sensitivity						Total Observed
	Negative		Doubtful		Positive		
	Observed	Expected	Observed	Expected	Observed	Expected	
1949	7	6	0	-	0	-	7
1950	63	62	0	-	7	8	70
1951	125	120	0	3	12	14	137
1952	96	95	3	3	9	11	108
1953	32	35	0	-	5	2	37
1954	7	7	0	-	0	-	7
Total	330	325	3	6	33	35	366

Table 9 presents the distribution of positive reactions according to the size and intensity of reactions, for the study group, the controls, and the entire Navy and Marine Corps. Here again the controls resemble the entire service fairly closely.

TABLE 9. *Degree of tuberculin reaction, positive reactors, study and control groups and all recruits, U. S. Navy and Marine Corps, 1949-1954*

Category	Reaction and per cent				
	1 plus	2 plus	3 plus	4 plus	Total
Study group	33.6	31.4	28.0	7.0	100.0
Control group	48.5	30.3	12.9	9.1	100.0
Recruits, U. S. Navy and Marine Corps, 1949-1954 (Chace)	50.2	28.8	15.7	5.3	100.0

Comparison of the study group of cases with the controls (or equally well, with all service personnel recruited in the 6-year period) reveals two important differences: (1) a much larger percentage of the cases were tuberculin positive at enlistment; and (2) when only the positive reactions are examined, there is a considerable excess of 3-plus (strongly positive) reactions among the cases.

It has been shown by Cornfield[12] that a comparison of the prevalence of an attribute in a case series with that in a control group can be made to yield an estimate of the relative incidence of the disease among persons in the population having, and those not having, the attribute. The validity of such an estimate depends on the extent to which the case series is representative of all cases of the disease in the population, and the control series is representative of the population itself. Reduced to its simplest form, the equation for deriving relative incidence of the disease from relative prevalence of the attribute may be expressed as follows:

$$\frac{\text{Incidence among persons possessing the attribute}}{\text{Incidence among persons not possessing the attribute}} = \frac{p_1 q_2}{p_2 q_1}$$

where p_1 and p_2 represent the prevalence of the attribute (in this case, tuberculin sensitivity on entry to service) among the cases and controls, respectively; and q_1 and q_2 represent the corresponding proportions of persons in the two groups who do *not* have this attribute. A condition for this equation is that the prevalence of the disease in the population must be small.

In table 6, it is shown that of persons whose tuberculin status on entry was known, 28.5 per cent of cases and 9.8 per cent of controls were tuberculin positive or doubtful. If one considers only those (enlisted) personnel who had negative chest x-ray findings on entry into service, the proportion of tuberculin reactors is essentially the same, 26.3 per cent of cases and 9.1 per cent of controls. Hence, the following values of p and q may be employed: p_1, 26.3 per cent; p_2, 9.1 per cent; q_1, 73.7 per cent; and q_2, 90.9 per cent.

These values, substituted in the above equation, lead to a rough estimate that the incidence of tuberculosis among tuberculin reactors was some 3.6 times that in the nonreactors. Unfortunately, the reactions of 21 per cent of the subjects are unknown, a fact which lessens the confidence in the estimate.

It was originally hoped to find specific information as to the length of time initially negative tuberculin reactors served before conversion. Immunization records showed, however, that periodic tuberculin testing after entry was a rare event, even among medical department enlisted men. In regard to the latter, it is possible,

of course, that local records of tests were not entered on the men's immunization registers. In any case, the time intervals between initial and subsequent tuberculin tests were essentially those between entry into service and final diagnosis, when tuberculin testing was again done.

In table 10 it is found that the median length of total service prior to coming under suspicion of tuberculosis was 28 months for the basic study group and 22 months for those of the study group who were tuberculin positive or doubtful on entry. This difference is significant and may be interpreted variously, one possibility being that some of the tuberculin-positive men were recently infected or in the prodromal stages of active tuberculosis on entry, Navy or Marine Corps service perhaps hastening the appearance of clinical disease. Another possibility is that these men had healed lesions on entry which reactivated early in training. Since the controls were matched to the study group by length of service prior to diagnosis, their median falls between these values.

TABLE 10. *Months of service prior to suspect diagnosis, by tuberculin reaction on entry into service, for male enlisted personnel*

Months of service	Cases				Controls*	
	Nonreactors		Reactors		Nonreactors	
	Number	Per cent	Number	Per cent	Number	Per cent
0-6	5	2.2	5	5.5	13	3.9
6-12	10	4.3	12	13.3	35	10.6
12-18	26	11.2	15	16.7	36	10.9
18-24	36	15.6	18	20.0	53	16.0
24-30	55	23.8	18	20.0	68	20.6
30-36	44	19.0	9	10.0	51	15.4
36-42	24	10.4	5	5.6	41	12.4
42-48	20	8.6	8	8.9	28	8.5
48 and over	11	4.7	0	0.0	5	1.5
Subtotal	231	100.0	90	100.0	330	100.0
Unknown	0		0		1	
Total	231		90		331	
Median (months)	28**		22**		26	

*The number (36) of reactors in the control group is too small to warrant distribution.
**P <0.001

The tuberculin status of men found to have nondisqualifying chest pathology on entry was investigated (table 11). It was noted that the term "tuberculosis" was rarely used in induction-film reports of men who were accepted with nondisqualifying chest pathology. It might be anticipated that positive reactors would show more chest pathology (Ghon tubercles, et cetera) than nonreactors. The figures for both the study group and the controls are in accord with this expectation. There is also, unexpectedly, a small but significant excess in the percentage of initially tuberculin-negative cases having x-ray findings "other than negative" on entry as compared to controls (3.0 per cent as against 0.3 per cent). A possible explanation for this difference is that a few men with chest pathology of tuberculous etiology were incorrectly read as negative reactors. Except for this, the correlation between tuberculin reaction and chest x-ray readings is in accord with expectation.

TABLE 11. *Results of chest x-ray on entry into service, by tuberculin reaction on entry, for all enlisted personnel*

Chest x-ray findings	Negative				Positive or doubtful				Unknown			
	Cases		Controls		Cases		Controls		Cases		Controls	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Negative	225	97.0	330	99.7	80	86.0	33	91.7	61	95.3	103	98.1
Other than negative	7	3.0*	1	0.3*	13	14.0	3	8.4	3	4.7	2	1.9
Subtotal	232	100.0	331	100.0	93	100.0	36	100.0	64	100.0	105	100.0
Unknown	1		1		0		0		6		10	
Total	233		332		93		36		70		115	

*$P < 0.05$

Note: Certain other comparable percentages on "other than negative" line are also significantly different. Thus, where 3.0 per cent vs. 14.0 per cent $P < 0.01$, and where 0.3 per cent vs. 8.4 per cent $P < 0.001$.

Place of Birth, Residence, and Population of Residence

The degree of uniformity of state of birth and of given residence on entry into service was first examined; for about 80 per cent of the persons in both groups they were the same.

A comparison of cases and controls by region of birth, employing the grouping of states into nine geographic regions used by the U. S. Public Health Service in its morbidity reports, disclosed no striking difference in the origins of the two groups.

The percentage of positive or doubtful tuberculin reactions by region of residence of enlisted men in the United States was studied but the number of reactors was too small for meaningful findings.

The study and control groups were classified according to whether their place of residence at the time of entry into service was a community with a population under 2,500, between 2,500

and 50,000, or over 50,000. Table 12 suggests that an increasing percentage of the controls were tuberculin positive with increase in community size. Since tuberculin status on entry has been shown to influence the probability of acquiring tuberculosis, it was necessary to control this factor when studying the effect of community size. Among nonreactors, the proportions of study and control persons who came from small and large communities were closely similar. In the case of positive reactors, there was some difference, but it was based on too small numbers to be meaningful.

TABLE 12. *Tuberculin sensitivity of control group, by population of residence on first entry into service, for all enlisted personnel*

Population	Number tested and read	Positive or doubtful reaction	
		Number	Per cent
Less than 2,500	120	8	6.7
2,500 to 50,000	123	10	8.1
50,000 and over	124	17	13.7
Subtotal	367	35	9.5
Unknown	1	1	
Total	368	36	9.8

Physical Characteristics

The heights and weights of all but three of the men under study were readily obtainable from accurate physical examination records made on first entry into service. The distributions are recorded in tables 13 and 14, omitting the three unknowns.

A comparison was made of heights and weights of the tuberculin-negative control group with a sample of 565 tuberculin-negative recruits processed through the U. S. Naval Training Station, San Diego, Calif., in 1949-1951.[13] The control group was slightly shorter than the San Diego group, the medians being 68.7 and 69.2 inches, respectively. The weights were in closer agreement. The San Diego group, of course, is less representative geographically than our control group, since this Training Center draws recruits mainly from the western, midwestern, and southern sections of the country.

The differences in height and weight between the basic study group and its control are noteworthy, and suggest that tall men and thin men were more at risk of developing tuberculosis. Again,

TABLE 13. *Height on first entry into service—male enlisted basic study group, by service*

Height in inches	Navy				Marines				Total			
	Study		Control		Study		Control		Study		Control	
	No.	%	No.	%	No.	%	No.	%	No.	% (cum.)	No.	% (cum.)
60 or less	0	0.0	2	0.8	0	0.0	0	0.0	0	0.0	2	0.6
61	0	0.0	1	0.4	0	0.0	0	0.0	0	0.0	1	0.9
62	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
63	5	2.7	5	2.0	0	0.0	4	5.1	5	2.2	9	3.6
64	6	3.3	10	4.0	0	0.0	1	1.3	6	4.8	11	6.9
65	5	2.7	22	8.7	2	4.3	7	9.0	7	7.9	29	15.7
66	12	6.6	21	8.3	5	10.9	7	9.0	17	15.3	28	24.2
67	17	9.3	41	16.2	6	13.0	8	10.2	23	25.4	49	39.0
68	25	13.7	40	15.8	11	23.9	13	16.7	36	41.2	53	55.0
69	31	17.0	28	11.0	7	15.2	15	19.2	38	57.9	43	68.0
70	26	14.3	25	9.9	4	8.7	10	12.8	30	71.1	35	78.6
71	25	13.7	24	9.5	7	15.2	9	11.5	32	85.1	33	88.6
72	16	8.8	16	6.3	2	4.3	2	2.6	18	93.0	18	94.0
73 or more	14	7.7	18	7.1	2	4.3	2	2.6	16	100.0	20	100.0
Total	182	100.0	253	100.0	46	100.0	78	100.0	228	100.0	331	100.0
Median (inches)	69.67		68.61		68.90		68.92		69.53		68.69	
Mean (inches)	69.10		68.34		68.74		68.19		69.06		68.30	
Std. deviation	2.60		2.81		2.13		2.41		2.52		2.72	
Std. error of mean	.193*		.177*		.315		.272		.167*		.149*	

*P <0.01

in comparing the percentage of deviation of weight from median weight for height standards on entry into service, a quite significant difference is noted in table 15 when all underweight categories are combined. The findings of these tables support the conclusion of Reed and Love[14] in their study of U. S. Army officers in 1933 that "The cases of pulmonary tuberculosis in young men are much more frequent among the thin ones, and especially the tall, thin ones." The same conclusion was reached by Long and Jablon[10] and by Palmer, et al.[11] Applying the formula $\frac{p_1q_2}{p_2q_1}$ it may be estimated from the data in table 15 that the incidence among underweight men was 1.8 times that among normal weight and overweight men. Similarly, the incidence among men 69 inches tall or taller may be estimated at 1.7 times that among shorter men. Both estimates are valid only if the control group is representative of Navy and Marine Corps personnel. It is be-

TABLE 14. *Weight on first entry into service—male enlisted basic study group, by service*

Weight in pounds	Navy				Marines				Total			
	Study		Control		Study		Control		Study		Control	
	No.	%	No.	%	No.	%	No.	%	No.	% (cum.)	No.	% (cum.)
Less than 90	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
90-100	0	0.0	1	0.4	0	0.0	0	0.0	0	0.0	1	0.3
100-110	4	2.2	4	1.6	0	0.0	2	2.6	4	1.8	6	2.1
110-120	7	3.8	15	5.9	3	6.5	4	5.1	10	6.2	19	7.8
120-130	22	12.1	30	11.8	1	2.2	9	11.5	23	16.3	39	19.6
130-140	38	20.9	41	16.2	17	37.0	13	16.7	55	40.4	54	35.9
140-150	44	24.2	50	19.8	9	19.6	22	28.2	53	63.6	72	57.7
150-160	34	18.7	46	18.2	6	13.0	9	11.5	40	81.1	55	74.3
160-170	21	11.5	30	11.8	3	6.5	10	12.8	24	91.6	40	86.4
170-180	4	2.2	18	7.1	3	6.5	4	5.1	7	94.7	22	93.1
180-190	6	3.3	9	3.6	3	6.5	2	2.6	9	98.7	11	96.4
190-200	1	0.5	4	1.6	0	0.0	2	2.6	1	99.1	6	98.2
200-210	1	0.5	5	2.0	1	2.2	1	1.3	2	100.0	6	100.0
Total	182	100.0	253	100.0	46	100.0	78	100.0	228	100.0	331	100.0
Median (pounds)	144.5		147.1		144.4		145.0		144.1		146.5	
Mean (pounds)	145.22		148.12		147.39		146.79		145.66		147.81	
Std. deviation	17.61		20.95		19.47		20.15		18.03		20.79	
Std. error of mean	1.304		1.315		2.870		2.282		1.194		1.143	

lieved that the evidence of the present study is especially convincing in view of the limitation of the comparison to personnel tuberculin negative on entry.

Entries as to body build noted on induction physical examinations were tabulated to see if there was any correlation with deviation of weight from the median weight for height findings already presented. The correlation was poor because it was evident that examiners seldom used the descriptive terms "heavy" or "obese" even in cases of rather marked obesity. The evident misapplication of body-build adjectives was too frequent to justify use of these data.

History of Venereal Disease in Relation to Tuberculosis

A record of venereal disease while in military service is one index of close contact with civilians, often of low socioeconomic status, among whom the prevalence of tuberculosis is likely to be high. The material was therefore examined for evidence of correlation between tuberculosis and venereal disease. Seventeen per cent of the male enlisted basic study group had a record of urethritis or of penile lesions following admitted sexual exposure.

TABLE 15. *Per cent of deviation of weight from median weight for height standard on entry into service—male enlisted basic study*

TABLE 15. *Per cent of deviation of weight from median weight for height standard on entry into service—male enlisted basic study group, by service*

	Navy				Marine Corps				Total			
	Cases		Controls		Cases		Controls		Cases		Controls	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Underweight												
More than 15%	23	12.6	28	11.1	5	10.9	10	12.8	28	12.3	38	11.5
10-14%	33	18.1	30	11.8	7	15.2	8	10.2	40	17.5	38	11.5
5-9%	44	24.2	41	16.2	13	28.3	17	21.8	57	25.0	58	17.5
All underweight	(100)	(54.9)	(99)	(39.1)	(25)	(54.4)	(35)	(44.8)	(125)	(54.8)*	(134)	(40.5)*
Normal												
Within ± 5% of median	60	33.0	84	33.2	14	30.4	24	30.8	74	32.4	108	32.6
Overweight												
More than 5%	22	12.1	70	27.7	7	15.2	19	24.4	29	12.7	89	26.9
Subtotal	182	100.0	253	100.0	46	100.0	78	100.0	228	100.0	331	100.0
Unknown	3		0		0		0		3		0	
Total	185		253		46		78		231		331	

$x^2 = 18.85$
$n = 2$
*$P < 0.001$

In the comparable control group, 15 per cent had a record of venereal lesions, an insignificant difference.

History of Contact with Tuberculosis

The induction medical history included questions as to familial history of tuberculosis but the reliability of the answers may be questioned. On the other hand, the information from clinical records of the study and control groups can hardly be contrasted, since questions as to exposure would naturally be stressed in history taking on a case of tuberculosis, while on a case of appendicitis this point would receive much less attention. Consequently, no comparison between the frequency of contact in cases and controls is justified. However, we may contrast (table 16) the frequency of a history of contact, prior to service, be-

TABLE 16. *History of contact with tuberculosis prior to service, by tuberculin reaction on entry into service, for all enlisted personnel*

Recorded contact	Tuberculin negative		Tuberculin positive	
	Number	Per cent	Number	Per cent
Study group				
None	191	83.0	56	60.2
Immediate family	22	9.6)*	25	26.9)*
Other	17	7.4	12	12.9
Subtotal	230	100.0	93	100.0
Unknown	3		0	
Total	233		93	
Control group				
None	295	96.4	30	85.7
Immediate family	7	2.3)**	4	11.4)**
Other	4	1.3	1	2.8
Subtotal	306	100.0	35	100.0
Unknown	26		1	
Total	332		36	

*P <0.01
**P <0.05

tween members of the study group who were tuberculin negative on entry and those who were tuberculin positive; and, similarly, the contact histories of tuberculin-negative and tuberculin-positive controls. Both comparisons reveal a higher frequency of contact among men whose tuberculin reactions were positive on entry. The majority of such recorded exposures were to persons in the immediate family. Among cases, familial contact was reported in 10 per cent of the tuberculin negatives and 27 per cent of the positives; among controls, in 2 per cent of negatives and 11 per cent of positives. It is impossible to evaluate this information in the sense of estimating what proportion of tuberculous illnesses were acquired as a result of exposure in the patient's home either before or during military service, but some of them undoubtedly were.

The Navy's intensive program of searching out and examining all known close contacts of tuberculous servicemen is reflected in the fact that 31, or 13 per cent, of the basic study group of cases gave a history of in-service contact with tuberculous service personnel.

[To be concluded]

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ESOPHAGEAL CORROSION BY ATTEMPTED SUICIDE IN THE ARMY

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CORROSIVE substances are not often utilized in suicide attempts in this era, the great majority of corrosive injuries being due to accidental ingestion. The amount of damage to be expected is worse when suicide is the intent, because even though a spontaneous reflex tends to cause quick ejection of the material from the mouth and throat in spite of the person's intentions, the subject bent on self-injury is likely to gulp the first swallow. This is because he expects the material to be unpleasant, and because there must always be a sudden last-minute impulse to go ahead with the act. Another important difference between suicidal and accidental cases is that the former are adults, while the latter are most often children.

This report deals with the study and treatment of 14 active-duty Army personnel who attempted suicide through ingestion of a corrosive substance.

THE PATIENTS

There were 11 men and three women in the group. Four were Negroes; the others, Caucasians. Five of the patients were between 18 and 21 years of age, five were 22 to 26 years, and one each was 35, 37, 49, and 58 years old. Three of the younger men attempted suicide just before Christmas, and two on the day before their birthday. All but two of the other attempts were made in the early spring or late winter. Eight of the patients had been drinking prior to ingestion of the corrosive agent, and it was believed that six of these had been drinking heavily. In each case it was concluded that a fairly serious attempt at self-destruction had been made. This is almost always the situation when agents of such generally recognized destructiveness are used for suicide.

From 2d General Hospital, APO 180, New York, N. Y.

THE AGENTS

Eight of the patients chose household lye, a mixture of sodium hydroxide and sodium carbonates, for suicide; four chose Drano, which approximates household lye in its corrosive composition; and two used an Army-issue cleaning compound composed of highly alkaline phosphates. Although it was often possible for the patient to indicate how much of the material he had taken into his mouth, this did not give much information regarding the injury, because expectoration, regurgitation, and vomiting had eliminated an unknown quantity after an unknown period of tissue contact.

INITIAL CLINICAL FINDINGS

All patients were examined within 32 hours of the poisoning, some within one hour. Five had had emergency first aid elsewhere. One patient was stuporous eight hours after having ingested household lye. The rest had severe pain in the mouth and throat. Odynophagia to the point of hydrophobia was encountered regularly. Deep substernal pain was a complaint of all, and in some it persisted many days. There were no complaints of epigastric pain or discomfort elsewhere in the abdomen. Three patients had stridor on admission; in one, this was severe enough to warrant an immediate tracheotomy.

Seven patients were vomiting blood upon admission and one, who apparently had aspirated some of the corrosive material, had hemoptysis for 18 hours. A ninth patient, first examined 32 hours after poisoning, vomited copious amounts of pink-orange pus without gross blood for 12 hours. Smears of the pus showed large numbers of square-ended bacilli, and cultures were positive for *Pseudomonas aeruginosa*. The other patients had ejected some of the corrosive and vomited briefly at the time of poisoning, but did not vomit thereafter.

On initial oral examination, maximum burn damage was found on the lips, tongue, soft palate, and uvula. Irregular ulcerations with a gray, filmlike slough were found within two hours of the poisoning. During the first two days these, and the hyperemic appearance around the ulcerated areas, changed very little except for gradual subsidence of underlying edema.

During the first 48 hours, all patients had some degree of fever. This reached a maximum of about 102°F in most cases. In two patients the fever lasted four days, and in another, six days.

Leukocytosis was a prominent laboratory finding. It usually persisted about a week. The highest count was 26,500 per μl, with 94 per cent neutrophils. The hemoglobin fell below 11 grams per 100 ml in nine patients, but in all cases the esophageal

bleeding was brief and return to normal hemoglobin values was spontaneous and relatively rapid.

PATHOLOGIC PROGRESSION

The progression of pathologic events within the esophagus was judged on the basis of serial roentgenographic, esophagoscopic, and transesophagoscopic biopsy studies, which were continued at one- to three-week intervals as long as the patients remained under personal surveillance. Although initial examination seemed to indicate that mucosal injury had been produced throughout the esophagus in all cases, the obscuring effects of edema, bleeding, and exudate production made accurate delineation of the areas of maximum damage very difficult early in the course (fig. 1). After the acute reaction had cleared, it was found that maximum injury had been sustained by the distal one third of the organ in three instances, by the middle one third in two, and by extensive scattered areas in the other nine.

The earliest endoscopic findings—on the third day—were constant from case to case. Regularly, there was severe mucosal edema, sometimes softly occluding the esophageal lumen as a diffuse process, sometimes being irregularly distributed along the organ's length. Patchily spread over the paleness of the edematous areas were varying degrees of hyperemia, often intense. Necrotic, irregular, superficial ulcers occurred with variable frequency and severity from patient to patient. Although heavy and thin gray exudate was found regularly in cases in which no gross ulceration was observed, both exudate and blood were so prominent when ulceration was present that the esophagoscopic picture was one of strikingly angry, chaotic, almost amorphous tissue destruction. Biopsy specimens taken at this earliest stage showed coagulation necrosis, intense inflammatory necrosis, acute inflammatory exudate, and masses of bacilli. Tissue showed no cellular detail (fig. 2).

At the end of the first week, the only important changes found in the two patients re-examined this soon were disappearance of active bleeding and decrease in the amount of free exudate in the lumen. Biopsy specimens, however, revealed a strikingly intense, acute inflammatory reaction with many bacteria, in wholly necrotic surface tissue.

By the end of the second week, esophagoscopic examination showed that a marked change had occurred in most cases. Now the mucosa was clean, and two features dominated the scene: The areas previously ulcerated were now filled in with soft dark-orange granulations, and those areas in which the epithelium had remained intact now appeared thick, leathery, and dead-white. Often in these cases the distal esophagus showed rather typical mild, nonspecific, erosive esophagitis, with tiny scattered

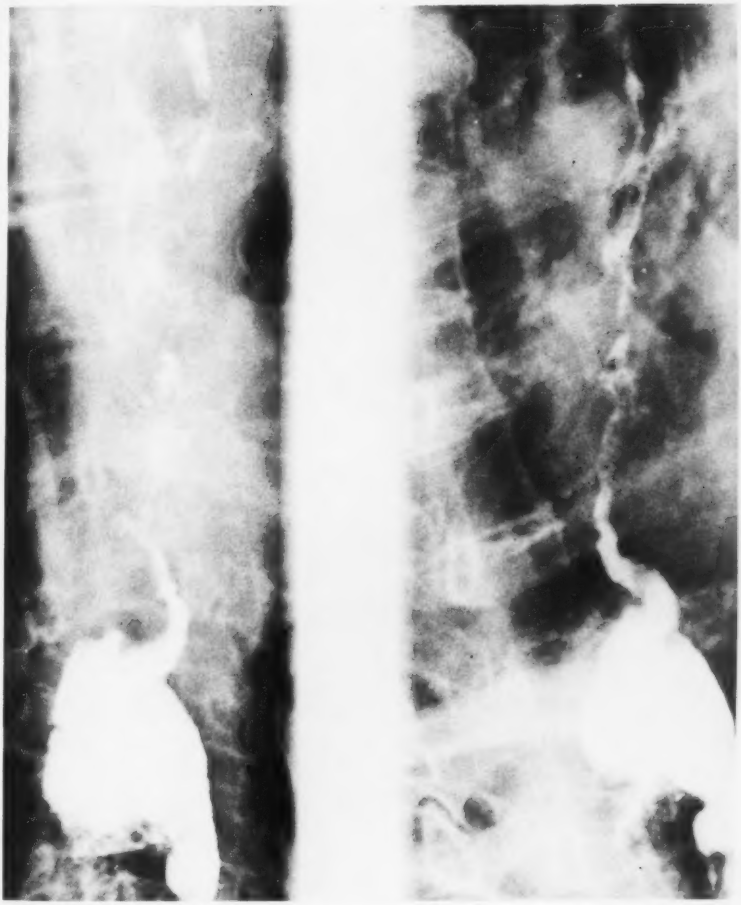

Figure 1. Roentgenographic findings four days after poisoning. The severe distortion is due largely to edema and spasm. On the same day a No. 40 French dilator was passed without difficulty.

erosions, a small amount of exudate, and hyperemia. Biopsy specimens at this stage showed coagulation necrosis of residual mucosa, with hypervascularity and acute inflammation beneath, and typical granulation tissue with beginning fibrosis elsewhere.

From this point on, the progression of events showed two predominant features: regression of inflammation and granulation, and progression of fibrosis. From the third week through the third or fourth month, however, great variability was found from patient to patient in the rapidity of these changes. In one patient,

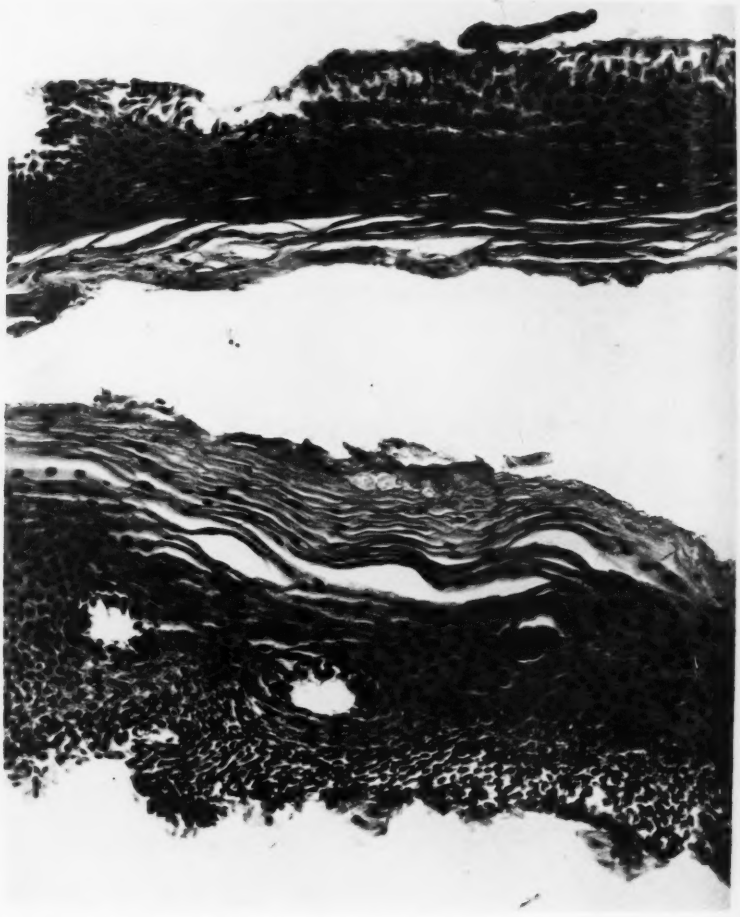

Figure 2. Biopsy of sloughed, coagulated epithelium, fourth day. (× 110)

successive biopsy specimens showed that granulation persisted for four months, gradually being replaced thereafter by hypervascular fibrous tissue, rich in fibroblasts. In other patients, beginning fibrosis was evident histopathologically a week after poisoning.

Although in all patients dilatations prevented clinically important stricture formation during the period of observation, a tendency to form strictures was observed regularly, both roentgenologically and esophagoscopically. This was first encountered three weeks after poisoning, as best the point could be

determined; however, the distinction between narrowing due to infiltration and edema and that due to actual stricture is not as easily made as one might guess. As time went on, it became evident that multiple strictures were the threat. In some cases, 10 or 12 areas of beginning stricturing could be identified. These areas of chronic repair for the most part corresponded to the areas of maximum acute injury. Some of the narrowings involved one half to two thirds of the length of the esophagus, while others were short and weblike (fig. 3).

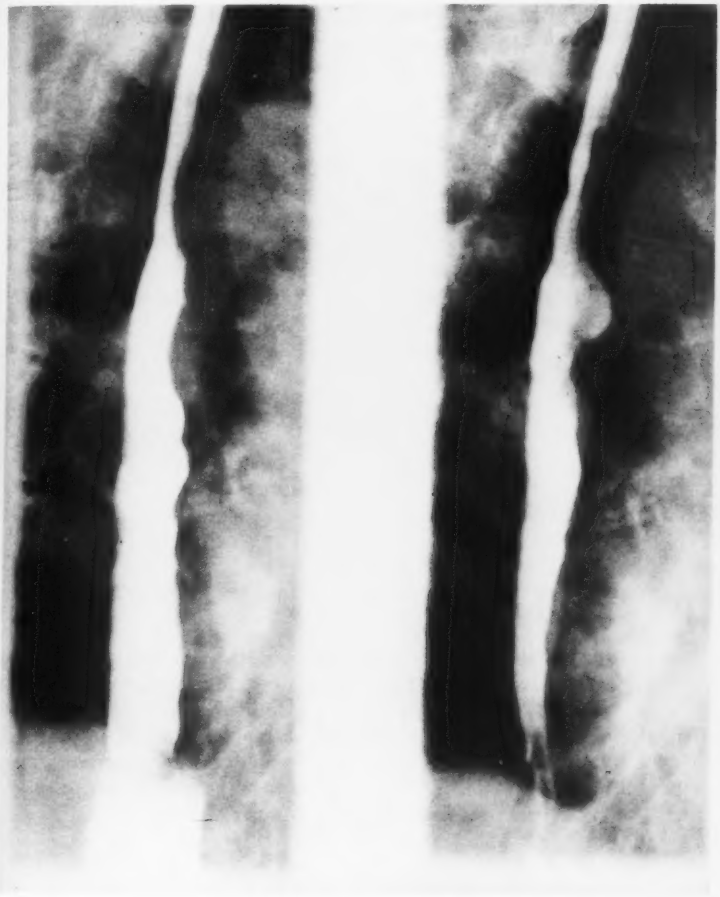

Figure 3. Roentgenographic findings eight weeks following poisoning. The distal one third of this esophagus was severely corroded. Extensive esophagitis is evident, but the lumen remains adequate and at this point accepted a No. 36 French dilator.

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TREATMENT

All patients were treated by a previously described modification of the Salzer technic.[1] Steroid therapy was used in only one case, with results already reported.[2] Briefly, the technic calls for passage of a Levin tube into the stomach as soon as the patient is encountered, both to maintain an esophageal lumen and to permit hydration and feeding. On the third day, the tube is withdrawn and esophagoscopic evaluation of the damage is made. Although this gives relatively little detailed information if the esophagus has been severely injured, it must be borne in mind that patients with severely burned mouths and throats may have sustained no esophageal injury at all—this is the point that early esophagoscopic examination must establish.

Immediately thereafter, daily dilatations are begun with Hurst mercury bougies, beginning with and if possible continuing with a bougie of large diameter, perhaps a No. 42 French. After about three weeks, the dilatations are carried out at less frequent intervals (three times a week; then twice a week, once a week, et cetera, but the patient must be kept under medical surveillance for years. During the first three weeks, large doses of penicillin and streptomycin are used, because secondary bacterial infection of the esophageal wall probably is as conducive as the corrosion itself to later fibrosis and stricture formation.

Although this is not an easy technic for patient or doctor, no special problems were met in this group of patients. It is particularly important to note that there were no complications from the transesophageal manipulations, for the technic has been criticized as dangerous. The most realistic danger is that of permitting strictures to develop. A conservative attitude which permits an esophagus to close off months or years later is reprehensible; an iatrogenic esophageal perforation in the course of sincere prophylactic ministrations is not.

The results of the present treatment could be judged personally over only relatively short periods, because after definitive treatment had been instituted the patients usually were transferred to a Veterans Administration hospital for the remainder of their course. Although personal observation averaged only seven months per patient, reports were received up to eight years in some cases. One patient died five months after the poisoning, of pulmonary embolus from bilateral lower extremity thrombophlebitis.

All of the patients responded satisfactorily to dilatations, none requiring gastrostomy or other surgery. The problems encountered in keeping the esophageal lumen open, however, were very difficult in some patients. Passage of a No. 42 French

bougie on the fourth day following poisoning was very easy. Ordinarily, no resistance was felt until about the tenth day. At that time it was common to find that suddenly the esophageal lumen seemed much narrower, now able to accommodate only a bougie of much smaller caliber. In one typical case of severe esophageal damage, the largest bougie which would pass through the entire length of the esophagus into the stomach from day to day from the fourth day on was as follows: No. 42 French, 42, 42, 36, 40, 40, 30, 30, 36, 36, 40, 40, 30, 32, 32, 32, 32, 30. In spite of loss of ground such as this, it was believed that dilatations could be carried out less frequently from this point on, both because biopsy studies show that the intramural pathologic processes have slowed down to a great extent by the beginning of the fourth week, and because it has been found that less frequent dilatations at this stage are effective in producing a gradual enlargement and in maintaining an optimum lumen. Thus, through the fourth, fifth, and sixth weeks in the case just cited, the maximum-sized bougie which could be passed on successive efforts was, respectively, No. 32, 36, 36, 42, 36, 36, 38, 42 French. The important thing is that dilatations, with periodic roentgen and endoscopic evaluation, be continued indefinitely. The patients throughout the course of treatment are swallowing well and see no reason for continued dilatations. It is this asymptomatic phase which is so dangerous, for fibrosis is gradually accumulating. The behavior of esophageal fibrosis is notably insidious in that following an insufficiently treated corrosive burn, stricture may not make itself known for many months or even years. Although, as stated, these patients were not followed personally to conclusion of their prophylactic dilatation therapy, it was thought that they were headed toward good eventual esophageal function, provided dilatations and periodic evaluation were studiously continued.

SUMMARY AND CONCLUSIONS

The clinical, pathologic, and therapeutic aspects of esophageal corrosion, as they were observed in 14 active-duty Army personnel who attempted suicide through ingestion of corrosive materials, have been reported, with emphasis on the safety, apparent effectiveness, and importance of early prophylactic dilatations.

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CASE REPORTS

Teratoma of the Thyroid Gland in an Infant

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MARCUS R. BECK, *Lieutenant Colonel, MC, USA*
WARNER F. BOWERS, *Colonel, MC, USA*

TERATOMAS of the thyroid gland are a rare finding. In a comprehensive review of the literature in 1935, Pusch and Nelson[1] were able to find only 28 cases of thyroid teratomas occurring in the newborn and infants. Potter[2] found that, although teratomas of the thyroid are rare, it is one of the more common tumors presenting in the newborn and frequently may produce dystocia or stillbirth. White and Gosselin[3] and Bale[4] reported on teratoma of the neck in the region of the thyroid gland; however, these cases were not considered histologically as arising from the thyroid gland.

The purpose of this article is to present a case of teratoma of the thyroid gland detected in an infant and treated with good results.

CASE REPORT

The patient was a 2-year-old male whose mother noted a small, soft, nontender mass in the anterior lower part of his neck about three months prior to his admission to this hospital on 25 April 1957. The mass had gradually increased in size. In retrospect the mother felt that the child's neck had always appeared fuller and thicker than she would have expected. The child had been noted to feed with difficulty on occasions and did not tolerate solid foods easily. He also had maintained a chronic, coarse, moist type of respiration, which the mother had attributed to an upper respiratory allergic condition. There were no other significant findings or events as related by the parents.

Physical examination revealed no abnormal findings except for the presence of a firm, rubbery, nontender mass just to the right of the midline at the base of the neck. The mass measured 2 by 2 cm on palpation. The patient's respirations were of a rasping, nasal quality. Urinalysis was negative, blood cell counts were within normal limits, and the roentgenogram of the chest was normal.

On 26 April under general endotracheal anesthesia, a low cervical collar incision was developed and the strap muscles divided. The mass was found to rest in the right thyroid fossa and was contiguous

From Tripler U. S. Army Hospital, APO 438, San Francisco, Calif.

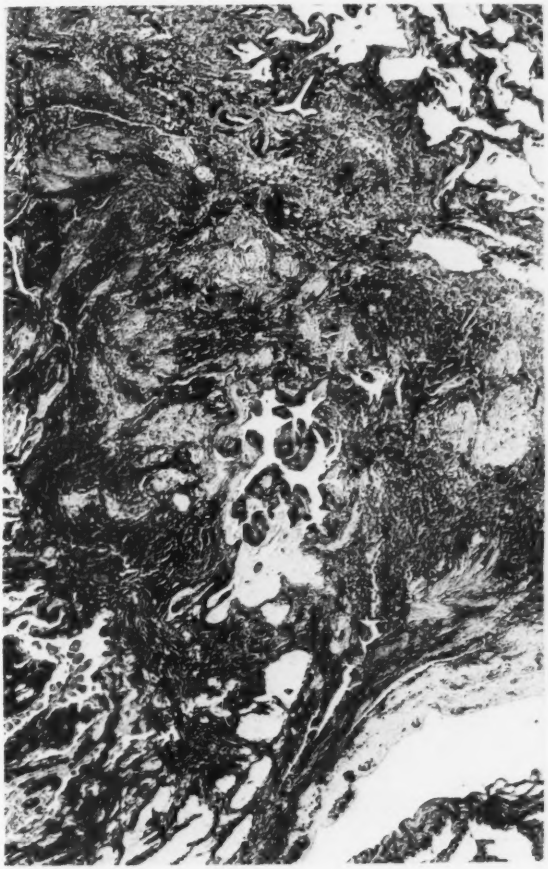

Figure 1. Photomicrograph of specimen showing the predominant features of the teratoma. Some of the cystic spaces are lined by glia and contain papillary projections. (× 10)

with the thyroid isthmus. The left lobe of the thyroid gland was normal in appearance. The lesion appeared to be encapsulated and was removed with the isthmus. The posterior enlargement of the mass was found to cause pressure on the trachea and esophagus. The immediate postoperative course was uneventful.

On return to the surgical outpatient clinic, the mother reported that the child's respirations were greatly improved and that his voice had lost its nasal quality. He was able to eat solid foods without difficulty and was experiencing no unusual symptoms. The patient continues

to do well and his growth and development are compatible with his age, 10 months after the operation.

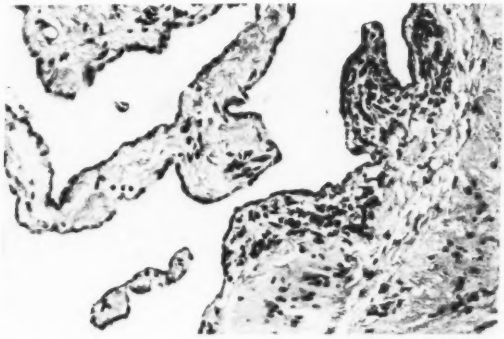

Figure 2. Photomicrograph of the cystic spaces lined by ependyma. These areas are similar to those found in cystic lymphangioma. (× 125)

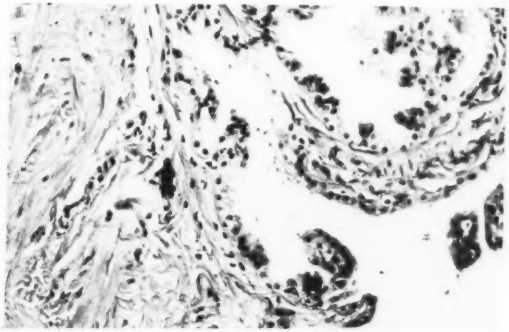

Figure 3. Photomicrograph showing papillary projections and smooth muscle noted frequently in the specimen. (× 125)

Pathologic Findings

The gross surgical specimen consisted of an oval, encapsulated brownish gray mass, 4.5 by 2.3 by 1.4 cm. While there were two cysts of 1 and 1.5 cm respectively, the bulk of the specimen was made up of small clefts containing clear fluid. It was soft and rubbery. The appearance was uniform throughout, there being no bone or cartilage.

Microscopically (figs. 1 and 2), lymphatic spaces were the predominant element, being identical to those found in cystic lymphangioma. Other spaces, however, were lined by normal appearing glia. Many cystic areas contained papillary projections (fig. 3), not infrequently related to glia. Rare inclusions of nonkeratinizing epidermoid cells were noted,

and there were a few microcysts lined by an indifferent cuboidal epithelium. These, while not positively identified, seemed more consistent with ependyma than with thyroid tissue. The teratoma contained no mucin-producing elements. All tissue elements appeared mature.

SUMMARY

Teratoma of the thyroid gland is rare. Such a tumor in a two-year-old boy caused difficulty in swallowing solid foods and in breathing, by pressing on the trachea and esophagus. Following surgical removal of the teratoma, the patient did well and there was no evidence of recurrence 10 months after the operation.

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CONTRAINDICATIONS OF WEIGHT REDUCTION

"It seems undesirable as a rule to attempt to reduce weight in children or pregnant women. A better solution consists in keeping the child's or the pregnant woman's weight at its existing value and letting the child "grow up" to the weight or letting postpartum weight loss achieve at lease part of the desired result in the pregnant woman. It is important to remember, when dealing with obesity in childhood, that inactivity may be the major cause and that it may be easier and more effective to step up activity than to reduce food intake. Care must be exercised, particularly with children obese since their youth, not to do more harm than good; with present methods, the prognosis for such subjects is generally poor and the psychological trauma of persistent and tactless attempts at reduction may be considerable."

—JEAN MAYER, Ph. D., D. Sc.
in *Bulletin of New York Academy of Medicine*
p. 758, Nov. 1957

Filariasis of Testis

ANTHONY A. BORSKI, *Major, MC, USA*
ROBERT R. TIPTON, *M. D.*

THE standard references to genital involvement by filaria usually describe epididymitis and orchitis as being most notable, with no reference to an isolated nodule of the testis.[1] Infection is initiated when the filariform larvae are introduced into or onto the skin by infected mosquitoes, especially *Culex fatigans,* the tropical house mosquito. This filarial infection is produced by *Wuchereria bancrofti,* a delicate, thread-like worm which lies in the lymph vessels and lymphoid tissues associated with the external genitalia. *W. bancrofti* does not multiply in its invertebrate hosts. Consequently, the number of mature larvae that can be transmitted by a mosquito is dependent upon the number of microfilariae ingested at the time of the infective blood meal.[2] The incubation period is one year, and may be symptomless. Microfilariae were found in 20.3 per cent of 2,421 Samoans upon the examination of a single sample of their blood.

A new concept of diffuse sylvan foci of transmission for non-periodic *W. bancrofti,* as contrasted with transmission in a domestic environment for the periodic variety of this human filarial parasite, was presented in 1955.[3] This explains why males have a greater infection rate and also why natives of open villages have statistically less infection than those in smaller or diffuse bush villages.

The pathologic basis for the acute and chronic stages consists fundamentally in cellular infiltration around the locations where immature or adult worms are present, and particularly when they become moribund, later die, and become calcified. Following the usual acute inflammatory reaction, the process is followed by fibrous encapsulation of the vessels in the locations where the worms have lodged. Fibrosis extends until elephantiasis develops. The lower extremities, genitalia, and glands in the groin are most frequently involved; however, the processes may extend into the bladder or peritoneal cavity.

Several thousand American troops were exposed to filariasis in the South Pacific in World War II.[4,5] About 20 per cent of

From Fitzsimons Army Hospital, Denver Colo.

the exposed individuals developed acute lymphangitis and lymphadenitis during the biological incubation period.[6] Many had localized funiculitis with or without epididymitis, orchitis, or hydrocele. Very few developed chronic sequelae. When examining biopsied lymph nodes of servicemen with filariasis, gravid female worms were recovered less than a year after the earliest date of exposure, although none of these men showed a microfilaremia.[7] Repeated exposure is required for the disease to become permanently disabling. A report of a case of filiarial infestation in a young Canadian soldier from the Korean theater of war was presented in 1955. Axillary lymph nodes were infested with the worms and no microfilaremia was found.[8] Prognosis is good for the servicemen who were exposed, but is poor for natives, who tend to develop permanent lymphatic obstruction. A relatively safe and orally administrable drug, Hetrazan (brand of diethylcarbamazine citrate), is capable of eliminating or greatly reducing the numbers of microfilariae in the peripheral blood.

We believe that all nodules of the testis should be surgically treated because 97 per cent are malignant.[9]

The following is a report of a case of filariasis of the testis, manifested by an isolated nodule.

CASE REPORT

A 33-year-old surgical technician was seen for evaluation of a painless nodule in the testis. He had never felt the nodule before, however, he had never searched for it until hearing the often-repeated remarks to interns about the necessity of bimanual palpation of testes, in order to detect lesions early. This lesion was found by a careful palpation of the testis by the patient.

Past history was significant. He was stationed in Samoa, New Hebrides, Guadalcanal, New Caledonia, and St. Mathias Group of Islands from June 1942 to December 1944. He was in the vicinity of of hundreds of natives with obvious elephantiasis. Despite precautions, he received many mosquito bites. He was not aware of any illnesses except some fungus infection of the scrotum. The past history otherwise was noncontributary. The physical examination findings were normal, except for a 0.5- by 1-cm, elevated, firm, painless nodule on the midpole of the testis. The epididymis was normal. At operation an encapsulated lesion was excised from the tunica albuginia. The remainder of the testis was uninvolved and therefore not removed. The pathologic diagnosis was filariasis. Microscopic section showed the worm encysted in a fibrocalcific lesion. (figs. 1 and 2)

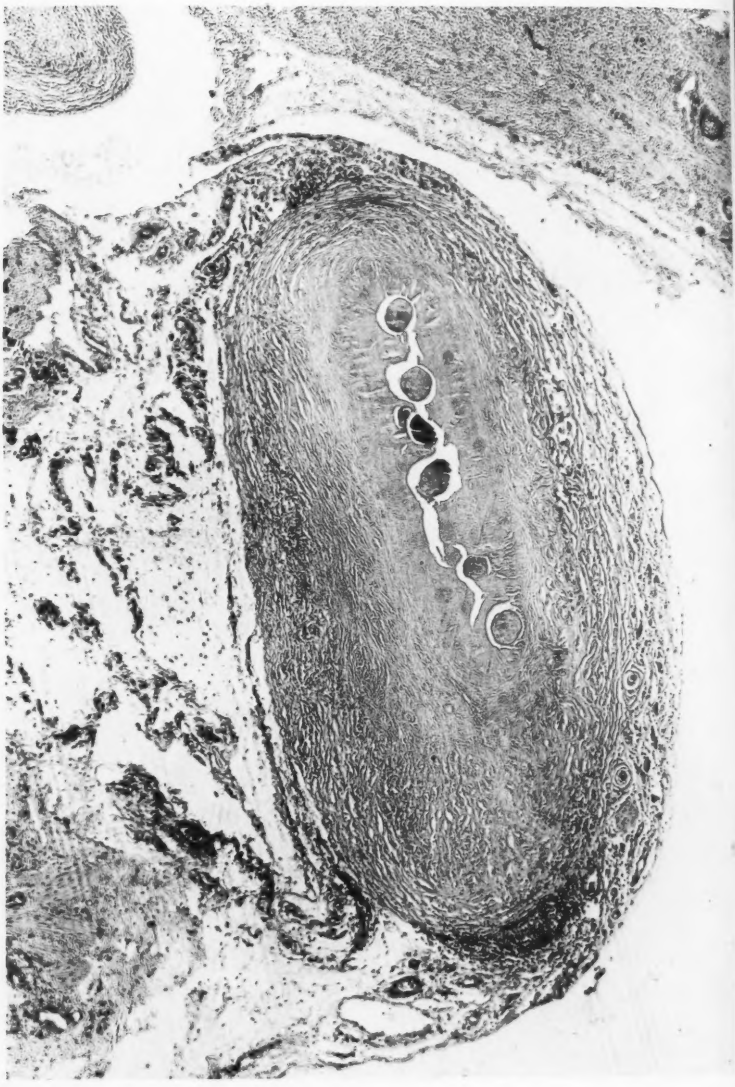

Figure 1. Low-power magnification through lesion, showing fibrosis, calcification, and several cross sections of the worm.

Figure 2. High-power magnification at area of calcification, showing cross section of the worm.

SUMMARY

A case of an isolated lesion of the testis due to filariasis is presented. No other manifestations of the disease were present. This adds another cause of benign lesions of the testis, however, it should not deter us from stressing the fact that all testis lesions should be considered malignant until proved otherwise.

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SUCCESS IN MODERN MEDICAL PRACTICE

"The young doctor of today is interested in his livelihood: in making a satisfactory living for himself and family. I am unable to reconcile to modern medical practice the time worn tradition that the doctor enjoys starving in his attic. It has always been my observation that a man virile enough to be a good doctor is also a hearty fellow who enjoys his food. Those sensitive souls who talk about one's love of science for science's sake and believe that those engaged in it do not claim an utilitarian value for what they accomplish have never had the administrative experience of a dean. The great men of medicine who have created epochs in the progress of science did not starve in laboratories, at least the court proceedings of their probated estates do not reveal many instances of such a tragic ending."

—A. C. FURSTENBERG, M. D.
in *Journal Medical Association of Georgia*
p. 512, Nov. 1957

An Unusual Complication Following the Use of Trilafon in Children

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SHELDON H. KAMIN, *Lieutenant, MC, USNR*
ALAN KLINE, *Lieutenant, MC, USNR*

DURING the past few years, tranquilizing agents have been used increasingly by physicians in various specialties. Of particular importance has been the endeavor to find drugs in the so-called "tranquilizer" sphere with minimal side effects and contraindications, together with a wide area of therapeutic indications.

One of the most recent additions to this field is Trilafon (brand of perphenazine). Like other phenothiazine derivatives, it is used in anxiety and tension states, in agitated psychoses, and in the treatment of schizophrenic patients. It also is considered to be a potent antiemetic. The purpose of this article is to report a rather unusual reaction in two children following the use of Trilafon.

CASE REPORTS

Case 1. A 10-year-old boy was seen in the outpatient department of this hospital, complaining of vague aches and pains in his extremities of several months' duration. According to the mother, he complained of "a new ailment" every day. He had been treated privately four years previously for "rheumatic fever." He also had been seen several years before, following a blow on the head as a result of which he was unconscious for several hours. Neurologic and electroencephalographic examination findings were reported as negative. Birth and development were described as normal and there was nothing unusual in his early emotional life. The mother stated that he was very intelligent, was "far advanced" in piano lessons, and that "he is all boy," indicating he was very active in the usual activities of his age group. A sister, a few years older was said to be "very emotional." His parents were somewhat confused, due to the fact that this very active, and apparently healthy, boy was continually complaining of physical discomforts. The physical examination and indicated laboratory findings were within normal limits.

From U. S. Naval Hospital, Jacksonville, Fla.

The child was started on Trilafon, 4 mg three times a day. Approximately 24 hours later, he was carried into the clinic, rigid, unresponsive, and appearing to be disassociated from his surroundings. He had taken the third dose of Trilafon that morning prior to going to school, and at school complained to his teacher of headache and stiff neck. Soon thereafter he was seen to stare fixedly, holding himself stiffly in his chair, immobile.

Shortly after his parents brought him to the hospital, the child was seen in neuropsychiatric consultation. He was lying rather rigidly on his side, with one leg elevated in extension and without motion. His face was expressionless and he looked fixedly into space. There was no meningismus. His head could be bent forward and backward with the type of resistance designated as "waxy flexibility." Moving the child's extremities was productive of the same bizarre mobility. Releasing the extremities resulted in fixational positions at levels in which they were released. There was no response to questioning and no outward show of pain. It was possible to move the patient into a sitting position, his head flexed back and his arms outstretched (fig. 1). Occasionally there was a Parkinsonian-like twitching of the thumb. The neurologic examination, including spinal fluid examination, was otherwise negative. The appearance of the patient was best described as cataleptoid, not unlike the picture of catatonia.

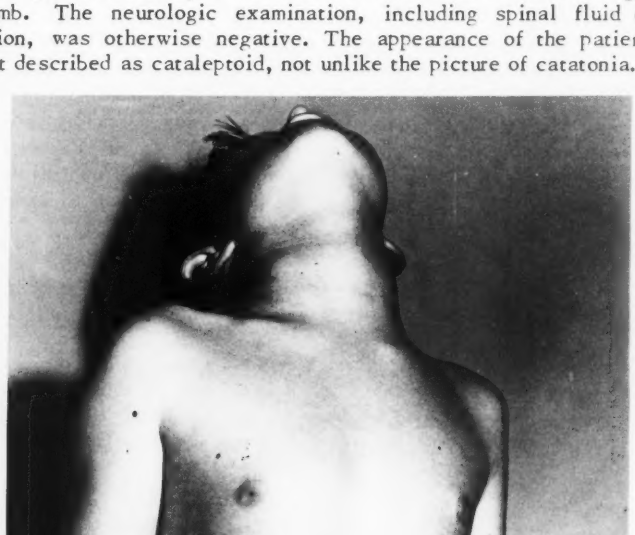

Figure 1 (case 1). Cataleptoid state following third dose of tranquilizing drug.

Approximately three hours after admission the child began to respond by moving his extremities on command but otherwise continued to be uncommunicative. During the night, brief episodes of torsion spasm were observed, but gradually these subsided and 16 hours after admission to the hospital he was entirely symptom free. His only remark in referring to his illness was "I was awfully afraid."

Case 2. A 6-year-old girl was seen in the outpatient department of this hospital for an upper respiratory infection. She gave a history of "earache" approximately a week before, during which she had a slight elevation in temperature, and her mother had kept her from school. The day before her visit to the clinic she had returned to school, but it had been necessary to send her home due to sudden onset of nausea, vomiting, and headache. At the clinic she was found to have a relatively mild upper respiratory infection. Because the nausea and vomiting continued, the patient was placed on Trilafon, 4 mg three times a day. The following day, after three doses of the medication, the patient complained of pain in the back of her neck, drawing her neck back. According to the mother, "her face pulled to one side." She "stiffened" and was brought to the hospital relatively immobile, speechless, and presenting the same picture as outlined in the previous case. She was seen in neuropsychiatric consultation and in addition to the above, the following history was elicited. She is the second of three children. Birth and development were outlined as normal. She is in first grade and, according to the mother, "she is the teacher's pet." Two weeks prior to admission, the child saw her father, who had been overseas, for the first time in seven months. He was home only for the night and was due to return home the night of the child's admission to the hospital. The child allegedly had missed her father greatly and "had crying spells about his being away." When the child started vomiting the morning of her initial visit to the clinic, the mother thought it was "a case of excitement" related to the fact that father would be home the following night. The mother described her daughter as "highstrung and sensitive but with the sweetest disposition."

Neurologic examination findings were essentially the same as in case 1. The child had a fixed stare, her features were immobile but did not express pain. The same "waxy flexibility" was elicited in all the extremities and in the neck. It was possible to sit the child upright and move her arms and legs to positions held without further motion. The neck tended to pull backward as though in spasm (fig. 2), yet it was possible to bend it fully forward and backward without eliciting any demonstration of pain. All indicated studies, including spinal fluid examination, were within normal limits. She remained immobile, with extremities in a semirigid position and with head pulled to one side for about four hours after her admission to the hospital. After this she gradually relaxed, and on command was able to move her extremities and to change her position in bed. Several hours later she became relaxed, fell asleep, and was discharged symptom-free the day following her admission to the hospital.

Figure 2 (case 2). Cataleptoid state following third dose of tranquilizing drug.

DISCUSSION

Both children reacted in a bizarre manner, requiring hospitalization, following three 4-mg doses of Trilafon. The outstanding symptom was a peculiar cataleptoid status with the phenomenon of "waxy flexibility" demonstrated in each case. Both recovered spontaneously approximately 12 hours after admission to the hospital.

A communication from the manufacturers of Trilafon,[1] indicated that the incidence of side effects in children has been reported to be very low, "far lower than in adults." The most frequent side effects were stated to be an increase in motor restlessness, a tonic spasm of certain muscle groups, particularly of the neck and face, these "spasms" responding to barbiturates and analgesics. They report only one case similar to our two cases; namely, a catatonic-like reaction in an 8-year-old boy, on 2 mg twice a day, occurring within 48 hours of administration of the drug.

The two cases presented here emphasize the fact that considerable caution should be used in the administration of tranquilizers, especially in children. Although, apparently, these

cases cleared up promptly without treatment, the traumatic psychologic effect on the parents witnessing their children in chemical strait jackets was undoubtedly severe.

It must be remembered that tranquilizers are potent drugs and that side effects will occur, especially in those individuals particularly sensitive to certain drugs.

REFERENCE

1. Personal communication from Schering Corporation, 60 Orange Street, Bloomfield, N. J.

ADVICE TO YOUTH ABOUT HEART DISEASE

". . .we are not yet on solid ground with respect to advice that we may give to the youth of tomorrow to avoid certain of the heart diseases of today, especially hypertension and severe coronary atherosclerosis. We may need another decade or two before we can speak with assurance. Perhaps the best advice is to carry out common sense measures that lead to a state of positive health and to support in full the important research of all possible causative factors that is in progress today and which will be developed more fully in the future.

"In the last analysis our goal is not to advise one single program of ways of life, i. e., environmental factors, for everyone, but to take cognizance also of the basic factors which concern the person, i. e., the host himself. We must fit the advice to the particular needs, and especially to protect the candidates from serious hypertension and coronary heart disease in youth and middle age. This goal therefore demands intensive research in heredity and other basic factors since they are at least as important as environmental factors acting as the agent. Thus the challenge is twofold."

— PAUL DUDLEY WHITE, M. D.
in *Bulletin of the New York Academy of Medicine*
p. 837, Dec. 1957

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CAREER PROGRAMS

"That the residency training programs furnish a major initial incentive for transfer to the regular Medical Corps of the U. S. Navy is evidenced by the fact that the majority of officers accepting such commissions during the past few years did so for the purpose of being assigned to those programs. Indications now point increasingly to the likelihood of a good majority of these men making a career for themselves in the Medical Department of the Navy. It will be a very happy and fortunate circumstance, indeed, if this pattern continues to prevail, for the so-called Doctors' Draft Law is just as unpopular with military authorities as with their civilian counterparts and with the profession of medicine at large in the United States. The only remedy for this difficult and trying situation is a potent nucleus of career medical officers. The Medical Department of the U. S. Navy, as well as of the U. S. Army and the U. S. Air Force, are urgently in need of the positive assistance and staunch support of all civilian physicians throughout the United States for the purpose of attracting a sufficient number of physicians to careers in military medicine to fulfill the critical responsibilities called for in our Constitution and in the Public Laws of the Congress. The potential catastrophic consequences of enemy thermonuclear, biological, and chemical warfare attack render it absolutely imperative that medical professional societies, organizations, institutions, and individuals everywhere in the country come forth with positive programs of action to help the Medical Departments of the U. S. Navy and her sister services accomplish their cardinal missions. The new Public Laws of the 84th Congress relating to military career incentives, dependent medical care, and survivors' benefits, including Social Security, all should attract more physicians to electing the military as a financially sustaining, professionally rewarding, and wholesome career."

—ROBERT B. BROWN, Capt., MC, USN,
MALCOLM W. ARNOLD, Capt., MC, USN
in *Archives of Surgery*
p. 252, Aug. 1957

ARMY MEDICAL RESEARCH ADVISORY GROUP HOLDS FIRST 1958 MEETING IN WASHINGTON

The Advisory Council on Research Affairs to the Surgeon General of the Army, Major General Silas B. Hays, held its first 1958 meeting in Washington on 21 and 22 March. Brigadier General Perrin H. Long, MC, USAR, Chairman of the Department of Medicine, Down-State Medical Center, State University of New York, presided at the conference which was attended by 8 members of the 11-man group.

Seated (left to right): Brigadier General Perrin H. Long, MC, USAR, and Major General Silas B. Hays, MC, USA; standing: Brigadier Generals Frank E. Wilson, James B. Mason, Manfred U. Prescott, Harold C. Lueth, Truman G. Blocker, Jr., Carl S. Junkermann, and Joseph M. Bosworth, MC, USAR.

Following the meeting, Brigadier Generals Alexander Marble, MC, USAR, Professor of Clinical Medicine, Harvard University School of Medicine, and Harold G. Scheie, MC, USAR, Professor of Ophthalmology, University of Pennsylvania School of Medicine, departed for two weeks' active duty training at the Brooke Army Medical Center, San Antonio, Tex. They will attend a special course in administration of a reserve hospital center.

NAVY'S CERTIFICATE OF MERIT GIVEN FOR SERVICE IN HEALTH AND SAFETY

One of the Navy Department's highest civilian awards, the Certificate of Merit, was presented to the CIBA Pharmaceutical Company recently in a ceremony in Washington. Representing the Secretary of the Navy, Assistant Secretary Fred A. Bantz presented the certificate to Mr. T. F. Davies Haines, president of the CIBA Company for outstanding service to the Navy Department in the fields of health and safety.

Assistant Secretary of the Navy Fred A. Bantz (left), Rear Admiral Bartholomew W. Hogan, and Mr. T. F. Davies Haines

During the ceremony, Secretary Bantz commented on the exceptional service that the CIBA Pharmaceutical Company has rendered to medicine and to the people of the United States in sponsoring one of television's notable educational series, "Medical Horizons."

The certificate contained the following citation:

For outstanding service to the Department of the Navy in the fields of health and safety. As sponsor of the television program "Man Under the Sea"—one of the "Medical Horizons" series—the CIBA Company brought great credit to the Navy and its Medical Corps. This coast-to-coast telecast from the U. S.

Naval Submarine Base, New London, Connecticut, depicted an unusual facet of the work of the Navy Medical Corps in showing how the health and safety of Naval personnel engaged in underwater activities is under constant medical observation. The nature of the story material served to inform the public that certain hazards are associated with the rapidly growing sport of scuba diving, and conveyed to the medical profession the nature of casualties and appropriate treatment as well as measures of prevention.

Also present at the ceremony were Rear Admiral Bartholomew W. Hogan, MC, USN, the Surgeon General of the Navy; other officials of the CIBA Company; representatives from the Bureau of Medicine and Surgery, Department of the Navy, Washington, D. C., and the U. S. Submarine Base, New London, Connecticut; and civilian physicians from the Washington area.

CAPT. HOUGHTON NAMED NAVY CHIEF NURSE

Captain Ruth A. Houghton, NC, USN, succeeded Captain W. Leona Jackson, NC, USN, as Director of the Navy Nurse Corps 1 May.

Born in Andover, Mass., Captain Houghton was graduated from the St. John's Hospital School of Nursing, Lowell, Mass., and received her Bachelor of Science in Nursing Education from Boston College. She has completed her work for the degree of Master of Science at Catholic University. She entered the Nurse Corps on 1 June 1935, and was appointed captain on 17 October 1957. She is a member of the American Nurses Association, the National League for Nursing, the Association of Military Surgeons, Sigma Theta Tau, and Pi Gamma Mu.

Captain Houghton

Captain Jackson retired on 30 April after a four-year assignment as Director of the Nurse Corps.

DEATH

HURST, Charles Wesley, Lieutenant Colonel, MSC, USAR, of Mackay, Idaho; stationed at Letterman Army Hospital, San Francisco, Calif.; served in an enlisted status in the United States Army from 4 March 1931 until 3 September 1934; commissioned in the United States Army Reserve 21 August 1938; ordered to active duty 26 September 1940; died 8 February 1958, age 43, at Colma, Calif., of a self-inflicted gunshot wound.

POSTGRADUATE PROFESSIONAL COURSES OFFERED ARMY MEDICAL SERVICE OFFICERS

The following Postgraduate Professional Short Courses for Army Medical Service Officers are announced for the first quarter, Fiscal Year 1959. Personnel interested and eligible to attend should apply through channels to The Surgeon General, Department of the Army, Washington 25, D. C. Attention: MEDCM-CG.

Advanced Military Preventive Medicine—Walter Reed Army Institute of Research, 14 July-18 October 1958

This course is designed to supplement the training given Army officers at civilian schools of public health by giving instruction in those aspects of preventive medicine and hygiene that are peculiar to the Armed Forces. A prerequisite is a master's degree in public health, or its equivalent, granted by a recognized civilian institution; and enrollment is restricted to officers continuing their careers in either preventive medicine or staff and command. Although the course is primarily designed for medical, dental, or veterinary officers; engineers, entomologists, and nurses who fulfill the entrance requirements will be accepted.

Radioisotopes in Medicine—Walter Reed Army Institute of Research, 14 July-10 October 1958

This course consists of three months' training in mathematics, physics, laboratory technics, and theory of diagnosis and therapy involving radioactive materials. The students will be required to take a refresher course in general physics and nuclear physics, as well as the applicable mathematics involving problem work. The theory of radioisotopes in medicine will be combined with actual patient contact in the radioisotope clinic. The course is designed to qualify medical officers in the use of radioisotopes in order to meet the requirements of the Atomic Energy Commission and for authorization for running radioisotope clinics in Class I and Class II installations.

Management of Mass Casualties—Walter Reed Army Institute of Research, 15-20 September 1958; Brooke Army Medical Center, 28 July-1 August 1958 and 22-26 September 1958

The purpose of the course is to indoctrinate officers of the military medical services in current concepts on the management of casualties resulting from the employment of nuclear weapons. The course is designed to provide current, up-to-date information of an unclassified nature on the medical aspects of nuclear warfare, to reduce this information to readily accessible and useful data in the solution of problems that might arise, and to stimulate thinking on ways of coping with the problem of casualties which might result from nuclear weapons.

Eleventh Symposium on Pulmonary Disease—Fitzsimons Army Hospital, 8-12 September 1958

The Eleventh Annual Symposium on Pulmonary Diseases will cover the diagnosis and treatment of tuberculous and nontuberculous diseases of the chest. Material will be presented in lectures, live clinics, and demonstrations, with emphasis on case presentations to small groups of participants. Demonstrations of technics of pulmonary function, bacteriologic methods, physical medicine, chest surgery, et cetera, will be provided.

Pulmonary Function Testing as Applied to Disability Ratings—Fitzsimons Army Hospital, 13 September 1958

This course is divided into afternoon and morning sessions. The morning session will be conducted in the laboratory with discussion of equipment and methods and demonstration of testing technics. Pulmonary function testing to be covered will be limited to the clinical type procedures, to include: external spirometer; measurements of flow rates; measurement of lung volumes and lung compartment relationships (open circuit nitrogen washout and closed circuit helium dilution); exercise measurements of ventilation and oxygen utilization (the work of breathing); oximetry (continuous recording type); and arterial blood gases (technic of Van Slyke measurements and pH determinations—Beckman Model G with special blood electrode).

The afternoon session will be devoted to a panel discussion on the use of physiologic tests in profiling disability in cardiopulmonary diseases. It will center around specific case presentations that illustrate various categories of pulmonary insufficiency and related disability. The cases will be selected from the pulmonary function clinic, Fitzsimons Army Hospital.

Medical Nursing—Walter Reed Army Institute of Research, 22-27 September 1958

This course is designed to provide an opportunity for nurses to appraise and plan for the needs of patients in the medical service for comprehensive nursing care applicable in Army situations. Emphasis will be placed on recent developments and trends in the clinical aspects of medical care and treatment of patients with selected disease conditions such as cardiovascular disease, endocrine disturbances, gastrointestinal disorders, communicable diseases, degenerative diseases, et cetera. In considering optimum nursing care for patients with these disease conditions, a portion of the time will also be devoted to the multidisciplined approach to care of patients and nursing team concepts; priority of care; continuing need for in-service education and on-the-job training; and implication for study and research to improve nursing care of medical patients.

Principles of Medical Operations in Nuclear Warfare—Walter Reed Army Institute of Research, 29 September-31 October 1958

This course is designed to teach selected medical officers the principles involved in medical operations in nuclear warfare, to include a review of mathematics and theory; nuclear weapons systems; phenomenology, and human effects; and medical plans, training and applications.

Current Trends in Laboratory Activities—Walter Reed Army Institute of Research, 8-13 September 1958

This course will present to Medical Service Corps laboratory officers recent advances in methods and the interpretation of results in biochemistry, bacteriology, serology, medical zoology, virology, and hematology. This will be augmented by an introduction to laboratory automation. In addition, certain aspects of atomic casualty studies of particular interest to the laboratory scientist will be presented. For the most part the material will be presented by the lecture-demonstration method. The student also will have an opportunity to acquaint himself with the technics of individual tests. The laboratories of Walter Reed Army Medical Center also will be available for consultation on individual problems.

OFFICIAL DECORATIONS

The following awards were recently announced by the Departments of the Army and Air Force.

Legion of Merit

Harry G. Armstrong, Maj. Gen., USAF (MC)* John H. Wilkins, Lt. Col., USAF (MC)
Marvin E. Kennebeck, Maj. Gen., USAF (DC)

Commendation Ribbon

Homer C. Knowlton, Capt., MC, USA

*Second Oak Leaf Cluster

First U. S. Meeting of WHO Begins 28 May

The World Health Assembly, the governing body of the World Health Organization, will hold its eleventh session in Minneapolis, Minnesota, beginning on 28 May 1958 and continuing for a period of three weeks. The United States will be host for this meeting, which will mark the tenth anniversary of the WHO, and the first time the delegates of the United Nations have held their deliberations in this country.

Dr. Sabih Hassan Al-Wahbi, former Minister of Health of Iraq, who was last year's president of the World Health Assembly, will open the 1958 session and preside until his successor is elected. Dr. M. G. Candau is Director-General of WHO.

A MESSAGE FROM THE A. M. A.

This is the second and concluding part of a report on the results of a continuing opinion survey of physicians released from active military service. The first part of this report appeared in last month's issue of the *U. S. Armed Forces Medical Journal*. This summary is based on 1,600 returns received in 1956. A total of 2,519 questionnaires were distributed by the Council on National Defense of the American Medical Association.

Physicians' Evaluation of Staffing Conditions. One of the questions was designed to obtain the opinion of physicians as to staffing conditions of nurses, enlisted medical personnel, physicians, dentists, and others at the two units where the physician served his longest and next longest assignments. With respect to the longest assignment, the tabulation of this multiple-answer question indicated that in the Army replies of overstaffing totaled 691, understaffing 823, and adequate staffing 1,470. In the Navy, overstaffing totaled 738; understaffing, 811; and adequate staffing, 1,415. The Air Force tabulation revealed 461 replies of overstaffing, 636 of understaffing, and 819 of adequate staffing. The response to the question concerning the next longest assignment revealed that in the Army, overstaffing totaled 671; understaffing, 701; and adequate staffing, 1,174. In the Navy the results were 697, 702, and 1,243, respectively, while the Air Force tabulation was 414, 473, and 710, respectively. Physician overstaffing in the Army and Navy and dentist overstaffing in the Air Force predominated in regard to the longest assignment, while physician overstaffing led in all three services with respect to the next longest assignment. On the longest assignment dentists and enlisted medical personnel were second and third, respectively, in regard to overstaffing in both Army and Navy, while physicians and enlisted medical personnel were second and third in the Air Force. On the next longest assignment dentists and enlisted medical personnel were second and third, respectively, in the Army and Air Force, while enlisted medical personnel and dentists were second and third in the Navy.

Unnecessary Aspects of Military Training. There were 477 physicians who responded affirmatively to the question, "Were there any aspects of your military training that were unnecessary or wasted?" Negative answers were received from 1,120 medical officers. Of those who answered affirmatively, the majority were of the opinion that nonmedical duties was the area of greatest waste in their military training. In the Army, 74 per

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From the Council on National Defense of the American Medical Association. The views and opinions expressed are not necessarily those of the Department of Defense. —*Editor*

cent of those who responded affirmatively were of that opinion, as were 37 per cent of those in the Navy and 73 per cent of those in the Air Force.

Making Military Service More Attractive. A total of 1,476 physicians offered suggestions for making military service more attractive for the practice of medicine. Only 124 physicians thought that nothing could be done to make military service more attractive to medical men. The leading suggestion of physicians in all three branches of the service was that there be an improved utilization of medical personnel. An increase in pay was the second most frequent suggestion from physicians in all branches, while higher rank with merit promotions was third as the suggestion of Army physicians, choice of stable location was third for the Navy, and more capable commanding officers was third for the Air Force.

Improvement of Services to Military Physicians by Medical Associations. A total of 515 physicians (32 per cent) offered suggestions in response to the question concerning the role of national and local medical associations in maintaining closer contact or rendering better service to their members who served as physicians in the Armed Forces. The other 1,082 physicians who returned the questionnaire offered no suggestions. The most frequently suggested improvements in services were: (1) more personal visits by civilian physicians to evaluate grievances, (2) more invitations to military physicians to civilian medical meetings, and (3) the dissemination of more information to military physicians.

Physicians Who Would Voluntarily Remain in Service. In response to the question relative to military service beyond the obligated tour of duty, 929 physicians indicated they would not be willing to stay in military service for more than two years under any conditions except total war. There were 671 physicians who indicated they would serve an additional period under certain conditions. Many physicians listed more than one condition. The most frequently listed condition was "increase in pay," followed by choice of stable location, choice of duty assignment, and opportunity to practice specialty.

Perferred Branch of Service for Practice of Medicine. There were 608 physicians who stated a preference for the Armed Forces in response to the question of preference if the physician were going to practice medicine in a Federal Government agency. A total of 971 physicians expressed a preference for other agencies of the Federal Government, while 18 physicians had no preference. Of those who preferred the Armed Forces, the vast majority chose the branch of service in which they had served.

Distribution by Rank at Time of Discharge. The majority of physicians in the Army and Air Force held the rank of captain at the time of their release from active military duty. However, in the Navy at the time of separation the majority held the rank of lieutenant, junior grade. There were 1,597 physicians who answered this question. The survey indicated that approximately 36 per cent of those who reported were in the lowest rank, while 44 per cent held the rank of captain (Army or Air Force) or lieutenant, senior grade (Navy). There were approximately 20 per cent with the rank of major or lieutenant commander, and higher.

Length of Active Service as Medical Officer. In the Army there were 600 responding physicians who served an average of 15½ months in the United States and 9 months at overseas stations. There were 614 Navy medical officers who had an average of 20 months of active duty in the United States and 5 months overseas. Responses from 383 physicians in the Air Force revealed an average tour of duty of 21 months in the United States and 6 months at overseas bases.

Reserve Status. Of the 1,597 physicians reporting, 806 indicated they retained their reserve commissions, while 788 resigned their commissions. There were 3 who did not respond. By services, the Army had 209 retaining commissions and 388 resigning; the Navy had 419 retaining and 195 resigning; and the Air Force had 178 retaining and 205 resigning their commissions.

OFFICERS CERTIFIED BY SPECIALTY BOARDS

Supplementary Listing

The following regular Medical Corps officers have been certified by the specialty boards indicated since the listings published in previous issues of this *Journal,* according to information from the Offices of the Surgeons General of the military medical services.

American Board of Orthopaedic Surgery

Richard H. Garrett, Maj., USA
Ernest R. Hartmann, Maj., USAF
David C. Kellsey, Lt. Col., USAF
James G. McFaddin, Maj., USA
James E. Nixon, Capt., USAF
Wilhelm A. Zuelzer, Lt. Col., USA

American Board of Internal Medicine

Jack C. Fitzpatrick, Maj., USA
William A. Frey, Capt., USAF
Robert L. Massonneau, Lt. Col., USA
Marshall E. McCabe, Lt. Col., USA

American Board of Surgery

David W. Aiken, Maj., USAF
Frederick B. Goslin, Capt., USAF
Bruce A. Raymond, Maj., USA

NAVY SCIENTIST GIVEN HIGH CIVILIAN AWARD

Doctor Clay G. Huff, head of the Division of Parasitology in the Naval Medical Research Institute, Bethesda, Md., recently was awarded the Navy Distinguished Civilian Award at ceremonies in the Office of the Assistant Secretary of the Navy Fred A. Bantz, for contributions in the field of parasitology, especially the malarial parasite, during the past 30 years.

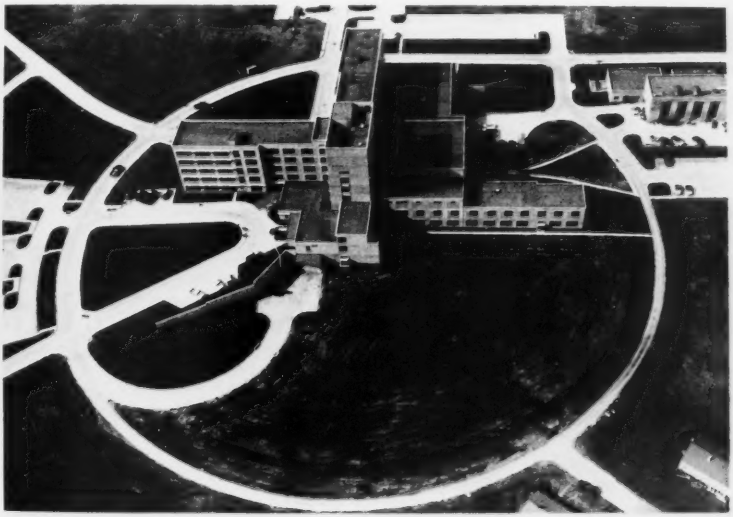
Assistant Secretary of the Navy Fred A. Bantz; Doctor Huff; Rear Admiral Bruce E. Bradley, MC, USN, Deputy Surgeon General of the Navy; and Captain Otto E. Van Der Aue, MC, USN, Commanding Officer, Naval Medical Research Institute.

Dr. Huff formerly was professor of parasitology at the University of Chicago. Since joining the Institute in 1947, his achievements have brought him recognition in the form of offices in several professional societies and the Theobald Smith Gold Medal awarded by the American Academy of Tropical Medicine for outstanding work in tropical medicine.

NEW HOSPITAL AT FORT RILEY NAMED FOR GEN. JOHN IRWIN, "THE FIGHTING DOCTOR"

The new Irwin Army Hospital, Fort Riley, Kans., named in honor of Brigadier General Bernard John Dowling Irwin, "the fighting doctor" and early winner of the Medal of Honor, was dedicated in an appropriate ceremony on 7 February 1958. Major General Silas B. Hays, Surgeon General of the Army, was the principal speaker.

Constructed in the latest military design at a cost of more than five million dollars, the new hospital is the third to be completed in the Army's program of modern medical facilities. The main building consists of five structurally separated units designed to provide medical service for 250 bed patients. It is expandable to a capacity of 500 beds by the construction of additional ward wings. The commanding officer is Colonel Milford T. Kubin, MC, USA.



Irwin Army Hospital, Fort Riley, Kansas.

The late General Irwin was born in Ireland on 24 June 1830 and received the degree of doctor of medicine from the New York Medical College. In 1856 he was commissioned in the Army medical service and served in New Mexico and Arizona. In an engagement with the Chiricahua Indians near Apache Pass, Ariz., in February 1861, he commanded detachments of Companies C and H, Seventh Infantry, and subsequently received the Medal of Honor for gallantry in action. He was post surgeon of Fort Riley on two occasions between 1866 and 1873. He was appointed Assistant Surgeon General of the Army in July 1892 and retired two years later. He died in 1917.

Reviews of Recent Books

CLINICAL HEART DISEASE, by *Samuel A. Levine,* M. D., F. A. C. P. 5th edition. 673 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $9.

The author is a colorful, well-known clinician and teacher who has not changed his purpose and goal in this fifth edition. He attempts to present the important aspects of diagnosis, prognosis, and treatment of heart disease in a simple manner, aimed primarily for the general practitioner. It is written in a narrative style, in the first person, with many references to clinical cases as if he were conducting a teaching conference. There is no bibliography.

This book has 22 chapters, each being a brief treatise on the subject under discussion. It was not intended to be comprehensive in scope or in detail. The chapter covering congenital heart disease was written by Dr. Alexander Nadas, who is an outstanding authority in this field. The chapter on electrocardiography covers 232 pages and was written by Dr. Harold D. Levine. A general introduction to vectorcardiography is incorporated into this chapter.

This book has many good features in the realm of clinical observation and general management of heart disease. There also are several drawbacks to this book. There is a tendency toward verbosity and rambling. While there is a great deal of excellent information in this volume, it is not organized for quick reference or review of the material.

The author discusses various elements of diagnosis, prognosis, and treatment in a general way, but this is not considered comprehensive enough for the serious student of internal medicine or heart disease.—*DOSS O. LYNN, Col., MC, USA*

THE YEAR BOOK OF OBSTETRICS AND GYNECOLOGY (1957-1958 Year Book Series), edited by *J. P. Greenhill,* B. S., M. D., F. A. C. S., F. I. C. S. (Honorary). 597 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1957. Price $7.50.

This pocket-size book is composed entirely of articles abstracted from journals published between July 1956 and July 1957. It is a comprehensive review of the literature covering that period and edited by a noted authority in the field. However, no mention is made as to the criteria used in selecting an article for inclusion. It must therefore be assumed that articles are included simply on the basis of their appearance in the literature during the time covered by the book. No attempt is made to evaluate the articles abstracted. In fact, the editor's notes consist of additional abstracts which in most instances do not bear on the previous article but deal instead with a different phase of the subject discussed. This criticism can, of course, be rendered impotent if the book is intended as a reference rather than a text. If the intention is that of a reference, then its value is in question from another quarter, namely, duplication of effort. Here

the reviewer makes reference to the fact that other publications are in existence with the same purpose. The busy practitioner no doubt prefers less duplication of effort by such authorities as J. P. Greenhill and more guidance to the valuable articles published so reading time can be used most wisely. —*J. WILSON HUSTON, Capt., MC, USN*

ADVANCES IN RADIOBIOLOGY, Proceedings of the Fifth International Conference on Radiobiology held in Stockholm on 15-19 August, 1956, edited by *George Carl de Hevesy, Arne Gunnar Forssberg,* and *John D. Abbatt.* 503 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $15.50.

This volume consists of 69 papers and covers the broad field of radiobiology, including fundamental effects at the cellular level, general physiology, including hematology, and genetics. A large section, more than one fourth of the papers, is concerned with the exciting new leads and modification of systemic radiation effects, including an exposition of the general principles, chemical methods, and the bone marrow work which has recently received much publicity. As in previous years, a number of reports have direct application for the clinical radiologist. These include isotope studies as well as problems with leukemia. In a particularly interesting paper Loutit reviews Kaplan's leukemia hypothesis as proposed in 1954, and a preliminary report by Faber from Denmark confirms earlier presumptive evidence of the association between clinical radiation exposure and leukemia.

The book is dedicated to H. J. Muller and contains 10 papers covering recent work in the field of genetics, including some human implications by T. C. Carter. The principles of back mutation, as well as modification in recovery from chromosomal damage are discussed. The nature of the proceedings are broad enough to be valuable to the clinician interested in radiotherapy and the treatment of cancer, and to the hematologist, radiation chemist, and radiobiologist.

—*JAMES B. HARTGERING, Lt. Col., MC, USA*

CARDIOVASCULAR REHABILITATION, edited by *Paul Dudley White,* M. D., *Howard A. Rusk,* M. D., *Bryan Williams,* M. D., and *Philip R. Lee,* M. D. 155 pages. The Blakiston Division, McGraw-Hill Book Co., Inc., New York, N. Y., 1957. Price $6.50.

This book is an edited publication of the proceedings of a conference on cardiovascular rehabilitation conducted under the sponsorship of the Institute of Physical Medicine and Rehabilitation of the New York University Medical Center. Thirty-five authorities in the specialities of cardiology, industrial medicine, physical medicine, and rehabilitation participated in the conference, and their views on the important aspects of cardiovascular rehabilitation are presented in an informal manner.

Work physiology, critiques of the various tests of evaluating cardiovascular work, and the physical, emotional, and environmental aspects of work as pertains to the cardiac patient are well presented. The

functions of work classification units and of State and Federal rehabilitation services are briefly summarized. Problems in the field of rehabilitation uncovered in the early discussions are then related to requirements for the teaching of cardiovascular rehabilitation, and emphasis is placed on those areas of present and future research that should be explored more fully. Of added value is the inclusion in the text of a comprehensive reference bibliography.

This timely, concise, yet comprehensive text is of definite value and will clarify for the reader the important problems of rehabilitation and management of the cardiovascular patient that are so often neglected in the usual texts. Its value is not limited to the industrial health specialist or cardiologist; rather its worth is equally applicable to those in all the fields of medicine.

—LOREN F. PARMLEY, Jr., Lt. Col., MC, USA

THE PRINCIPLES AND PRACTICE OF DIATHERMY, by *Bryan O. Scott*, M. R. C. S., L. R. C. P., D. Phys. Med. 193 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $5.

For physical therapists, and others who require a clear and concise text on the fundamentals of short-wave diathermy, this volume is valuable. The physics of this method of deep-heat therapy are clearly and comprehensively covered. The author wisely limits the content to the technical aspects of application and does not attempt to delineate pathologic conditions amenable to short-wave diathermy. Included in this work are 18 chapters. The longest is devoted to technics concerning the regional application of this method of treatment. This reviewer has observed that this is a poorly understood subject but a noteworthy contribution has been made here. The many illustrations and diagrams are valuable and the simple explanations of technical terms make for lucidity and objectivity. Teachers of physical therapy will find this short volume ideal as a textbook for students who are seeking to acquire basic facts on short-wave diathermy.

—BENJAMIN A. STRICKLAND, Jr., Col., USAF (MC)

THE RELATION OF PSYCHIATRY TO PHARMACOLOGY, by *Abraham Wikler*, M. D. 322 pages. Published for the American Society for Pharmacology and Experimental Therapeutics by The Williams and Wilkins Co., Baltimore, Md., 1957. Price $4.

This book is a review in which an attempt has been made to survey the literature from 1930 to 1955 for material dealing with the effects of drugs used in psychiatry in the treatment or investigation of the "functional" behavioral disorders. This is an immense task, and, as the author points out, the "present review may be regarded only as an attempt to survey the problems which will have to be resolved in the future." The drugs reviewed are limited primarily to insulin, carbon dioxide, barbiturates, amphetamine and methamphetamine, pipradrol, chlorpromazine, reserpine, meprobamate, et cetera. The book is divided

into two sections; one on the "Effects of Drugs on Human Behavior," and the second on "Theories and Mechanisms of Drug Actions." Some repetition of material occurs in these two sections, but this adds to the value of the review.

For so difficult and complex a subject, the author has prepared a well-organized and easily read review, and he has included in one book much of the important work in this field. An adequate index adds to the usefulness of the book.—*SAMUEL V. THOMPSON, Capt., MC, USN*

PRACTICAL ALLERGY, by *M. Coleman Harris,* M. D., F. A. C. P., and *Norman Shure,* M. D., F. A. C. P. 471 pages; illustrated. F. A. Davis Co., Philadelphia, Pa., 1957. Price $7.50.

The authors have achieved a noteworthy accomplishment, namely, that of writing a book which fits the title perfectly. Material is presented in a manner that makes it easy to assimilate and utilize in the ordinary practice of medicine and the practice of allergy, by the nonallergist as well as the specialist in this field. Just the right amount of theory and controversial material is presented to indicate just how little is known in allergy, yet how much we can do for our patients despite this.

A good portion of the book is directed at the details of completing skin tests, desensitization technics, and specific and nonspecific therapy. In a book of this size it is impossible to be all inclusive, and great detail in theory is not indulged in; but the material is covered in sufficient degree to be useful and informative.

This book is intended for the general practioner and the nonallergist internist who thinks he would like to practice allergy. It should assist materially in this endeavor.—*DAVID L. DEUTSCH, Lt. Col., MC, USA*

AN ATLAS OF FETAL AND NEONATAL HISTOLOGY, by *Marie A. Valdes-Dapena,* B. S., M. D. Foreword by *Edith L. Potter,* M. D. 200 pages; illustrated. J. B. Lippincott Co., Philadelphia, Pa., 1957. Price $11.

This small atlas consists of a series of photomicrographs detailing the changing histologic structure of organs during fetal and early infancy. All of the illustrations are in black and white. In most instances there is sufficient detail to be useful to the pathologist and the student as a reference for normal structures. The pattern of the book has a descriptive text on the left-hand page with the photographs on the right. This form is more difficult for quick reference than, for example, the section on the kidney which has the caption for the data under each photograph. An excellent bibliography accompanies each section. The book suffers from the lack of an index and it is somewhat awkward to use until one becomes familiar with its contents. Pathologists and histologists should find this atlas a useful reference guide in the complexities of the normal histology of the developing fetus and the neonatal period.—*FRANK M. TOWNSEND, Col., USAF (MC)*

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ROENTGEN DIAGNOSIS OF ABDOMINAL TUMORS IN CHILDHOOD, by *Charles M. Nice, Jr.*, M. D., Ph. D.; *Alexander R. Margulis*, M. D.; and *Leo C. Rigler*, M. D. 75 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $4.

Dr. Rigler and his fellow workers from the University of Minnesota Medical School make a worthwhile contribution to the field of roentgen diagnosis by stressing the importance of making an accurate preoperative diagnosis in cases of children with abdominal tumors. He states that a large number of such masses may be accurately evaluated by relatively simple clinical and roentgenologic methods using a minimum of manipulation and expenditure of time, and affording the child much benefit and little harm.

The monograph discusses the importance of topographic location of masses in the abdomen and means of localizing such masses. The various landmarks and their displacements are described and a roentgen classification is offered. Their relative incidence in childhood and infancy is discussed.

The 75-page volume is beautifully illustrated by line drawings of body sections and schematic presentations as well as excellent reproductions of radiographs with plain films and using contrast materials showing various displacements by tumors. A comprehensive bibliography is included for those wishing to continue the subject. The book is highly recommended especially as a teaching aid for radiologists, oncologists, pediatricians, surgeons, and general practitioners who may deal with children.—*SYLVESTER F. WILLIAMS, Capt., MC, USN*

TUBERCULOSIS, Every Physician's Problem, by *J. Arthur Myers*, M. D. 290 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $7.50.

This book was written "for physicians in every phase of medical practice," and covers the subject broadly. It is very readable and presents the material in a personal manner. While other authors are freely quoted they all, not unnaturally, seem to support the viewpoint of the author. Some subjects are presented in such detail, that in a book of its size other perhaps equally important material must be slighted.

On some matters the author is quite opinionated, i. e., the use of BCG vaccine. In his zeal to dispose of this subject he neglects to give any consideration to some seemingly reliable reports from many different investigators. Dr. Myers does, however, show dramatically what can be done in tuberculosis control without use of attempts at immunization. His documentation of tuberculosis control methods in Minnesota is fascinating and the excellent results of the program attest the significance of his contentions. The sections on control methods, the use of the tuberculin test, and his "offensive attack on the tubercle bacillus" are well worth reading. Those concerning the clinical aspects and treatment of the disease are sketchy, at best, with undue emphasis

on certain subjects while neglecting more important ones. The book presents background material on the subject of tuberculosis, which may well be read with profit by anyone interested in tuberculosis, but I cannot recommend it for a guide to diagnosis or treatment.

—*JAMES A. WIER, Col., MC, USA*

THE MERCK VETERINARY MANUAL, A Reference Handbook of Diagnosis and Therapy for the Veterinarian. 1,385 pages, thumb-indexed. Merck & Co., Inc., Rahway, N. J., 1955. Price $7.50.

This first edition is an excellent reference handbook of diagnosis and therapy for the veterinarian as well as others interested in diseases of animals. It is patterned after the *Merck Manual of Diagnosis and Therapy*, and incorporates the advances in form and style made by that publication since 1899. Some 200 contributors co-operated in its preparation. The arrangement of the contents in parts and sections with a list of chapter titles and subtitles at the beginning of each section, the complete index with cross listings, and the alphabetical thumb index make it a convenient and timesaving reference. The basic parts of the book present the following broad topics: Diseases of large and small animals including nutrition; toxicology, including herbicides, insecticides, bacterial toxins, and chemical poisons; diseases of poultry; health and disease problems of animals maintained in laboratories, on fur farms, and in zoos; and an addendum with public health and other useful ancillary information. The listing of an editorial board would give greater authority, and specifically naming contributors would add considerably to the value of the material. The reviewer believes that this publication will prove most popular and useful to the doctor of veterinary medicine, as the *Merck Manual* has been to the physician.—*ROBERT R. MILLER, Col., USAF (VC)*

THE YEAR BOOK OF PEDIATRICS (1957-1958 Year Book Series), edited by *Sydney S. Gellis*, M. D. 469 pages; illustrated. The Year Book Publishers, Inc., Chicago, 11, Ill., 1957. Price $7.50.

Edited again by Dr. Sidney Gellis, the 1957-1958 Year Book of Pediatrics brings to the reader a thoughtful selection of articles appealing to the practicing pediatrician. The sections on the premature and newborn and nutrition and metabolism are good, and statements by guest commentators round out some controversial articles.

Under infectious disease and immunity, a number of extremely interesting articles are presented. The gastrointestinal and genitourinary tracts receive excellent coverage, as well as those on the cardiovascular system and blood. With the present emphasis on screening of murmurs and congenital heart disease, pertinent articles will find more interested readers. A number of very good articles are included in the section on endocrinology, together with some good illustrations. Orthopedics receives adequate space, including discussions on steroid therapy in transient synovitis of the hip. The reader will find some absorbing articles on neuropsychiatry. Allergy

and dermatology are rather briefly presented, and dentistry and otolaryngology barely mentioned.

Illustrations are fairly numerous and of fair to good quality. Comments by the editor are succinct and interesting. Discussions by a few of the "guests" are at times verbose and take up space, perhaps better devoted to additional articles. Emphasis continues to be given to articles of immediate use and current interest. A very worthwhile book.—*MILTON KURZROK, Capt., MC, USN*

THE LOWER URINARY TRACT IN CHILDHOOD, Some Correlated Clinical and Roentgenologic Observations, by *Sven Roland Kjellberg, Nils Olof Ericsson,* and *Ulf Rudhe.* 298 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1957. Price $18.

The authors have presented in an excellent manner the variations of normal and the abnormalities of the lower urinary tract in children. The subject material consists of children age 1 day to 15 years, totaling 1,461 cases, seen or treated by them.

The text begins with separate chapters on embryology, anatomy, and physiology, which are beautifully portrayed with excellent illustrations and reproductions of x-rays. These sections are very complete and easily understood, which in itself makes the book worthwhile. Subsequent chapters consider each abnormal entity encountered in children separately, again with many fine reproductions of urethrograms and cystograms which are correlated with the text. Most of the abnormalities described are congenital in origin, as expected, and under each heading, the authors present their treatment and results of such treatment. Many cases are presented with excellent x-rays showing the findings initially, during treatment, and after treatment. The only topics not discussed in this book are hypospadias, epispadias, and and exstrophy of the bladder which were treated by the plastic surgery units in Stockholm.

I believe this book is an excellent addition to the growing list of texts on urology. It should be read and studied by all urologists, pediatricians, and general surgeons who see some of these unfortunate children usually when irreversible damage to the urinary tract has already occurred. An excellent reference table at the end of the textbook should be invaluable for any one wishing to study separate topics in more detail.—*NICHOLAS MALLIS, Maj., MC, USA*

DIGITALIS, Compiled and edited by *E. Grey Dimond,* M. D. 255 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $7.

This monograph is an outgrowth of a two-day postgraduate program on digitalis given in February 1956 at the University of Kansas Medical School. The material presented by representative investigators provides fairly complete coverage of the digitalis glycosides, encompassing their history, pharmacology, physiology, experimental approaches, toxicity, and therapeutic use. This compilation suffers somewhat from

the usual defect, namely, lack of editing as concerns style and ease of expression, so common to books of multiple authorship. Better portions of the text are found at the beginning and the end. It begins with the classic description of digitalis by William Withering as reprinted from Major's "Classic Descriptions of Disease," and ends with a panel discussion, moderated by the editor, which contains much information of practical value.

In summary, this book adds to the organized knowledge in cardiology. The bibliography given by each discussant is comprehensive and authoritative. Its use is recommended by internists and cardiologists. The book can well be made part of the hospital professional library.

—*ARCHIE A. HOFFMAN, Col., USAF (MC)*

THE POSTOPERATIVE CHEST, Radiographic Considerations after Thoracic Surgery, by *Hiram T. Langston,* M. D., *Anton M. Pantone,* M. D. and *Myron Melamed,* M. D. Publication No. 11, The John Alexander Monograph Series on Various Phases of Thoracic Surgery, A Memorial to John Alexander (1891-1954), edited by *John D. Steele,* M. D. 228 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1958. Price $8.

This is another volume in the extremely fine John Alexander Monograph Series on various phases of thoracic surgery. This great surgeon is being honored by his students and associates with the high tribute of these monographs which will be of great interest to all of those engaged in thoracic surgery. This particular volume presents the radiographic considerations after thoracic surgery. The reproductions of the x-ray films are extraordinarily good and are accompanied with clear line drawings and a brief clinical summation with radiographic interpretation. This is an unusual book and unexcelled.

—*JAMES H. FORSEE, Brig. Gen., MC, USA*

AN INTRODUCTION TO MEDICAL MYCOLOGY, by *George M. Lewis,* M. D., *Mary E. Hopper,* M. S., *J. Walter Wilson,* M. D., and *Orda A. Plunkett,* Ph. D. 4th edition. 453 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1958. Price $15.

This is the fourth edition of this important book. Previous editions have been the work of Lewis and Hopper; however, this one bears the names of two additional coauthors, Wilson and Plunkett. This is a practical treatise on fungus diseases and documents both clinical aspects and laboratory characteristics of the various pathogenic fungi. Common contaminants are also discussed. All material is presented in a logical, concise, clear, and readable style.

A major change has been made in the format of this edition. The clinical and laboratory phases are no longer separated but are considered together in the same chapter. Each of the pathogenic fungi is presented in this manner. In addition, the authors have taken the first steps toward replacing clinically descriptive terms by etiologic ones, believing that this is the proper approach in the description of disease processes. Illustrations are an essential and valuable part

of this book. They deal especially with the clinical manifestations of the diseases, the laboratory characteristics of all the pathogenic fungi, and the most commonly encountered contaminants.

Medical mycology is steadily increasing in practical importance. The proper management of fungus infections requires specific knowledge of their clinical pictures and their etiologic agents. Inasmuch as most organs and systems may be attacked by one or more of the pathogenic fungi the reading of this book is recommended to all practicing clinicians, especially dermatologists, internists, chest surgeons, and general practitioners. Medical mycologists will find it an important and reliable standard laboratory reference volume.

—JOHN W. ALBRITTAIN, Capt., MC, USN

PEDIATRIC CLINICS OF NORTH AMERICA, November 1957, Symposia on: I. Pediatric Endocrinology, *William A. Reilly*, M. D., Consulting Editor. II. Brain Damage in Children, *James G. Hughes*, M. D., Consulting Editor. Pages 801 to 1167, including Cumulative Index for Years 1955, 1956, and 1957; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1957. Price $15 per year of four books issued quarterly (February, May, August, November). Sold only on a yearly basis.

The general excellence of the Pediatric Clinics of North America is further attested to by this volume. Further, it illustrates the almost uncanny ability of the publishers to choose for their clinics subjects of particularly current interest. In both pediatric endocrinology and problems of organic brain disease in children, clinical interest and research have, in the last few years, reached an all-time high. Because of the large volume of material relative to these subjects that has appeared recently, the average physician has been outdistanced in his ability to keep apace with recent developments. The current volume of the clinics will do much to bring the reader up to date.

Of especial value to the practicing pediatrician are the chapters devoted to the methods of diagnosis and the laboratory procedures available to aid him in his investigations. The technics of the tests of various endocrine function are not covered but clear statements on the reliability, value, and limitations of the determinations are given.

Of special interest, too, because of the attention directed to the subject in the lay press, are the chapters on intersexuality. Not only is the material of value to the clinician for the assistance he can gain in the investigation of these problems, but there is a large amount of related information which should prove helpful in discussing these problems with parents.

The symposium on brain damage in children is more in the nature of a review of what is known about the factors leading to cerebral palsy, epilepsy, and related diseases. Current therapeutic measures are discussed and the effectiveness of all of the newer sedative preparations evaluated. *—DANIEL STOWENS, Maj., MC, USA*

DENTAL CLINICS OF NORTH AMERICA, November 1957. Symposia on: I. Tumors of the Oral Regions, *Hamilton B. G. Robinson*, D. D. S., M. S., Consulting Editor. II. Modern Practice in Endodontics, *Robert G. Kesel*, D. D. S., M. S., Consulting Editor. Pages 619 to 924; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1957. Price $14 per year for three numbers (March, July, November). Sold only on a yearly basis.

This third of a series of publications is equally as informative as its predecessors, and is interestingly and readably written. It encompasses two distinct areas in dentistry, tumors of the oral regions and endodontics, reported by 28 contributors thoroughly qualified in their respective fields. First a broad picture of the problem of oral tumors is presented, including views on etiology, diagnosis, prognosis, treatment, and post-therapeutic prostheses. Discussions are confined to the anatomic regions of the oral cavity. For example, one participant describes tumors of the tongue and floor of the mouth, and another tumors of the buccal and labial mucosa. Consequently, similar types of tumors which might be found in various regions are discussed several times. This gives the reader the viewpoints of several authorities. The latter chapters are devoted to a comprehensive study of endodontics, each by a different author. The chapters are so arranged that they describe in a very orderly manner the current practices in the selection of teeth for root canal therapy, diagnostic procedures, and the various treatments involved in restoring teeth which have diseased pulps. Well-written and well-illustrated, this book should attract many readers among practicing dentists.

—*VERNON S. FRICKE, Lt. Col., USAF (DC)*

CLINICAL ELECTROCARDIOGRAPHY, The Spatial Vector Approach, by *Robert P. Grant*, M. D. 225 pages; illustrated. The Blakiston Division, McGraw-Hill Book Co., Inc., New York, N. Y., 1957. Price $7.50.

There is a definite need for this book inasmuch as it presents electrocardiography in readily understandable and clinically practical form. Beginners in the interpretation of electrocardiograms as well as medical internists and cardiologists should find this book of great value. Dr. Grant presents his text as the result of several years of experience in research electrocardiography, combined with a keen appreciation of the clinician's viewpoint.

The format of this book is clear and logical with the subject presented in eight chapters, beginning with the theory and method of vector electrocardiography, and closing with a chapter on the electrocardiogram in childhood and in congenital heart disease.

The author explains that the vector approach to electrocardiography does not replace the ordinary "pattern" interpretation of electrocardiograms but rather supplements the reading of perplexing or borderline tracings. The vector is used as a way for integrating and schematizing the information contained in the various leads of the clinical tracing. Consequently it is a graphic chart with no relation necessarily to the cause of the condition producing the particular tracing. Dr. Grant be-

lieves that with the spatial vector approach it is not necessary to "explore" nonconventional regions of the chest in search of diagnostic patterns or to use intraesophageal or intracavitary V leads.

The author emphasizes that an abnormal electrocardiogram is only an electrical sign of heart disorder, therefore is not diagnostic of any histologic or pathologic process. We all know severe congestive heart failure cases with normal electrocardiograms. The electrical interpretation of electrocardiograms is more accurate than their clinical interpretation.

Dr. Grant prefers the designation "pre-excitation" with a delta wave to describe the Wolff-Parkinson-White syndrome, since the latter is sometimes associated with other nonspecific abnormalities.

I believe this book is of definite value to any physician practicing internal medicine primarily. The approach to the diagnosis of myocardial infarction and the discussion of the arrhythmias and tachycardias are especially well presented. —*U. R. MERIKANGAS, Col., MC, USA*

LIVER-BRAIN RELATIONSHIPS, by *Ian A. Brown*, M. D., Ph. D. 198 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $6.50.

This well-known author, Associate Professor of Neurology, University of Minnesota, is a well-established personage in the field of neurology. In this concise monograph he discusses the many pertinent and intimate relationships that exist between the liver and brain, concluding with certain possibilities, speculations, and conclusions. Originally presented as a thesis at the University of Minnesota in 1953, the material has been re-expressed in the light of recent observations pointing up the inadequacies of our test parameters which will have to be improved before more positive correlations can be made.

The liver is reviewed historically, followed by case studies with and without hepatic coma. Several chapters on clinical studies discuss the various cerebral manifestations of hepatic disease, including hepatoencephalomyelopathy with and without coma, episodic transient hepatoencephalomyelopathy, and hepatolenticular degeneration (Wilson's disease). Pathologic aspects of these conditions follow.

The author conservatively discusses the liver-brain relationships without necessarily advocating or supporting any particular one, emphasizing throughout the necessity for an open-minded approach. The following relationships are considered: the biochemical defects in hepatic coma, the lack of clinical-laboratory-pathologic correlation in liver disease and brain disease, the central nervous system in liver disease short of hepatic coma, ammonia metabolism, glutamic acid metabolism, electroenceophalography in hepatic coma, the role of the blood-brain barrier, and biological abnormalities in hepatolenticular degeneration.

This publication is timely, authoritative, and emphasizes the need for research in this area. The material presented together with the selected references furnish an adequate background for the subject, and warrants careful perusal especially by the neurologist and internist who are apt to confine themselves too closely to their own respective fields without keeping abreast of advances in others. It may even be suggested that the psychiatrist who numbers many alcoholics among his patients might well profit by the clinical-laboratory-pathologic background presented. To these busy individuals, this monograph is heartily recommended.—*RICHARD R. CAMERON, Col., MC, USA*

THE YEAR BOOK OF GENERAL SURGERY (1957-1958 Year Book Series), edited by *Michael E. DeBakey,* B. S., M. D., M. S. With a section on Anesthesia, edited by *Stuart C. Cullen,* M. D. 560 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1957. Price $7.50.

This valuable volume contains representative articles from the world's surgical literature, published between May 1956 and May 1957, abstracted in a most understandable manner. The selection and grouping of the abstracts reveal current trends in the field of surgery. The volume is appropriately sectioned, has a complete table of contents, and is completely and accurately indexed. Meticulous and authoritative editorial judgment is evidenced in the selection of articles. The illustrations are ample and clear. Of additional value to the reader are the editorial comments scattered throughout the book; they help in evaluating the material presented and sometimes supplement the points in the basic abstract. This volume is worth buying, reading, and retaining by any physician.—*OAKLEY K. PARK, Lt. Col., USAF (MC)*

MANUAL OF PEDIATRIC PHYSICAL DIAGNOSIS, by *Lewis A. Barness,* M. D. 195 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., 1957. Price $4.

This manual can be reviewed in three or four hours. It should make the art of pediatric physical examination most enjoyable and revealing.

The first four pages dealing with the approach to the patient during the examination are especially valuable. It is presupposed that the reader has a basic knowledge of physical examination methods and terms. The manual is therefore geared to significant signs unique to the pediatric patient. Throughout the manual the author conveys two major impressions: (1) Emphasis is not on the organ system but the patient as a whole; (2) the pediatric examination is truly dynamic and variable within the pediatric age group, *i. e.*, a physical sign specifically abnormal if *absent* at a certain age is likewise abnormal if *present* at another age. This is the chief factor that makes pediatric evaluation different from the adult physical examination. The last six pages summarize 40 nosologic disease entities easily forgotten, but recognizable by characteristic general appearance, facies, or posture.

—*LEO J. GEPPERT, Col., MC, USA*

SHOCK AND CIRCULATORY HOMEOSTASIS, Transactions of the Fifth Conference, 30 November, 1 and 2 December 1955, Princeton, N. J., edited by *Harold D. Green*, M. D., D. Sc. 337 pages; illustrated. Josiah Macy, Jr. Foundation, New York, N. Y., 1957. Price $4.75.

This book should prove intriguing for all medical readers. The goal of the conferees in the Josiah Macy meetings—promotion of communication, exchange of ideas, stimulation of creativity among the participants—is adequately fulfilled. Throughout the book the authors are interrupted freely and lively discussion ensues. The multiplicity of graphs and charts make reading slow to correlate them with the text. There is a discussion on the effect of aureomycin on the ferritin system of the liver in shock and a study of the mechanics of deterioration of the peripheral circulation during protracted hypotension following induced hemorrhage. The substance related to hyperactivity observed initially (VEM), of renal origin, and the hepatic factor (ferritin VDM) which is seen with hyporeactivity, are thoroughly discussed. Hypothermia as a means of protection against shock is studied in dogs, given chlorpromazine and cooled, who showed a survival rate of 68 per cent as compared to 4 per cent of the controls and the feeling is expressed that survival may have been due to hypotension and decrease in bleeding. Chlorpromazine may influence the amount of hypotension that the dog tolerates, allowing a longer period of hypotension; organs are subjected to less stress because the residual blood circulates more effectively. This book is good basic reading for surgeons, internists interested in hemodynamics, and others doing work in the field of trauma.

—*ARCHIBALD G. M. MARTIN, III, Lt. Col., USAF (MC)*

OFFICE GASTROENTEROLOGY, by *Albert F. R. Andresen*, M. D. 707 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $14.

Major advances in knowledge, technic, and drugs have led to revolutionary changes in the practice of many of the medical specialties and subspecialties within the last few years. Although gastroenterology still awaits its revolution, so many advances have been made all along the line that a single author probably cannot give an accurate and balanced discussion of the entire field. Doctor Andresen is a distinguished and revered physician who has spent a lifetime in the practice of gastroenterology, and has been especially interested in the role allergy plays in the production of symptoms and diseases of the intestinal tract. He has here attempted to write a small book, based on personal experience, presenting "simple and specific information regarding gastrointestinal diseases and their treatment." No explanation is given concerning the choice of the title; the scope and method of presentation are rather conventional and cover hospital as well as office management. The book is in five sections. The first section, "a plan of attack on gastrointestinal diseases," explains the author's methods of history taking, examination, and treatment, and the reasoning behind his methods. Section II covers "diseases affecting the entire gastrointestinal tract" and contains some good advice on managing the acute abdomen.

Sections III and IV are devoted to disorders of the individual parts of the gastrointestinal tract, liver, gallbladder, and pancreas. The final section is concerned with "general diseases with manifestations in the gastrointestinal tract;" tuberculosis, syphilis, cardiovascular diseases, et cetera.

As would be expected, the best part of this book is that devoted to gastrointestinal allergy. Discussions in other areas suffer somewhat from brevity but, more important, contain many statements not in accord with generally accepted opinion and practice. The cause of peptic ulcer is said to be a local necrotic reaction in the stomach or duodenum, due to allergy to a noxious substance absorbed for distant foci of infection. One is cautioned not to transfuse patients bleeding from esophageal varices or duodenal ulcer, for shock is nature's way of controlling hemorrhage, and intravenous infusions will raise the blood pressure, dislodge the clot, and bleeding will recur.

The book is beautifully printed and bound, has a 27-page table of contents and an excellent 66-page index. Written as a "once-over lightly" survey, it would be more useful if it had not also been written "off the cuff." For those who can distinguish the author's idiosyncracies, this book contains a great deal of value. I do not believe that it can serve as the only gastroenterology text in a physician's library.

—BENJAMIN H. SULLIVAN, Jr., Col., MC, USA

VERTIGO AND DIZZINESS, by *Bernard J. Alpers*, M. D., Sc. D. (Med.) Modern Medical Monographs, No. 15, editor-in-chief: *Irving S. Wright*, M. D. 120 pages; illustrated. Grune & Stratton, Inc., New York, N. Y., 1958. Price $5.

This is the 15th in a series of the Modern Medical Monographs and takes up a subject of general interest to all in the field of medicine. This little volume with 100 pages of text is divided into 7 sections dealing with anatomic basis of vertigo, the labyrinth and its connections, physiology of the vestibular system, production of vertigo symptoms and signs, causes, diagnosis and treatment. It is followed by an 11-page bibliography which thoroughly covers the literature on the subject, and articles of special interest and importance are marked with an asterisk to facilitate selection.

In general, this little volume is well organized, easy to read and covers the various aspects of vertigo with thoroughness and competence. Very little adverse criticism can be leveled at the book, except for possibly the price which seems somewhat high. However, considering that the value of books cannot be measured in terms of their weight, in all probability this one is worth the price. This book will be of interest not only to the neurologist, but also to the otologist, the student of neurology and to those in general practice and internal medicine. There is probably no place in the medical literature at the present time where the subject of vertigo and dizziness is treated so comprehensively and, at the same time, concisely.

—ROY E. CLAUSEN, Jr., Lt. Col., MC, USA

MEDICAL JURISPRUDENCE AND TOXICOLOGY, by *John Glaister,* J. P., D. Sc., M. D., F. R. S. E., F. R. F. P. S. (Glasgow), in collaboration with *Edgar Rentoul,* M. B. E., M. A., LL. B., M. B., Ch. B. 10th edition. 720 pages; 225 illustrations, 72 in color. The Williams & Wilkins Co., Baltimore, Md., 1957. Price $10.

The wide acclaim received by this book is evidenced by the fact that the first edition was published in 1902. Although the current tenth edition has been fully revised with the inclusion of new material, the actual content has been reduced by some thirty pages. The problems of British medical jurisprudence are thoroughly reviewed, but have definite application to those occurring in the United States. Forensic pathology is handled in an interesting manner by the presentation of classic case examples for which the British are noted. Considerable detail is given to the problems of toxic substances and their detection. From the standpoint of forensic science in the United States, this book might serve as a useful adjunct, but should not be used to supplant the basic texts used in this country which present the problems of forensic pathology and their implications in the light of legal problems encountered in the United States.

—*VERNIE A. STEMBRIDGE, Maj., USAF (MC)*

MANAGEMENT OF THE HANDICAPPED CHILD, Diagnosis, Treatment and Rehabilitation, edited by *H. Michal-Smith,* Ph. D. Foreword by *Arnold Gesell,* M. D. 276 pages. Grune & Stratton, Inc., New York, N. Y., 1957. Price $6.50.

The present volume is a revision and re-titled edition of Pediatric Problems in Clinical Practice, Grune and Stratton, 1954. As stated by the editor its "purpose has been to present an authoritative survey in the sciences and community services which affect those children needing special assistance, treatment and habilitation."

For this reviewer, it has been difficult to ascertain the reading public for whom the book is intended. While it might be informative to professional personnel who work closely with children, such as child psychiatrists, clinical psychologists, and social case workers, it is, on the whole, written at a level below the understanding which such persons should already have. Further it does not seem particularly helpful to parents of handicapped children since much of its information would be provided to them by a specialist consulted in behalf of their child. The technical information appears to be above the level of most parents and little is stated in terms of what can be done to assist the specialist once treatment is initiated.

In my opinion the major usefulness of the book is as a reference text for "survey" type courses or prescribed reading for persons beginning their training in such fields as social case work, public and private school teaching, pediatrics, clinical psychology and child psychiatry. Its final chapter might well be read by persons in local communities interested in establishing or co-ordinating services for handicapped children.—*JAMES W. LAYMAN, Lt. Col., MSC, USA*

New Books Received

Books received by the *U. S. Armed Forces Medical Journal* are acknowledged in this department. Those of greatest interest will be selected for review in a later issue.

ULCERATIVE COLITIS, by *Harry E. Bacon,* B. S., M. D., Sc. D., LL. D., F. A. C. S., F. A. P. S. Foreword by *Alton Ochsner,* B. A., M. D., Sc. D., F. A. C. S., F. A. P. S. (Hon.), with contributions by *Paul T. Carroll,* B. S., M. D. Chapter on Anesthesia by *Leroy W. Krumperman,* M. D. 395 pages; 184 illustrations. J. B. Lippincott Co., Philadelphia, Pa., 1958. Price $15.00.

PHARMACOLOGY IN MEDICINE, A Collaborative Textbook, edited by *Victor A. Drill,* Ph. D., M. D. 2d edition. 1,273 pages; illustrated. Published by McGraw-Hill Book Co., Inc., Blakiston Division, New York, N. Y., 1958. Price $19.50.

ABDOMINAL OPERATIONS BY THE VAGINAL ROUTE, by *Paul Werner,* M. D., and *Julius Sederl,* M. D. Translated by *L. M. Szamek,* M. D., with a Foreword by *Richard W. TeLinde,* M. D. 165 pages; 120 plates. J. B. Lippincott Co., Philadelphia, Pa., 1958. Price $9.00.

THE ESSENCE OF SURGERY, by *C. Stuart Welch,* M. S., M. D., Ph. D., and *Samuel R. Powers, Jr.,* A. B., M. D., M. Sc. D. 320 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $7.

THE STORY BEHIND THE WORD, Some Interesting Origins of Medical Terms, by *Harry Wain,* M. D. 342 pages. Charles C Thomas, Springfield, Ill., 1958. Price $8.50.

CLINICAL PROCEDURES IN OCCLUSAL REHABILITATION, by *S. Charles Brecker,* D. D. S., F. A. C. D. 326 pages; 936 illustrations on 428 figures. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $16.

SELECTED EXPERIMENTS IN MEDICAL MICROBIOLOGY, by *Stewart M. Brooks,* M. S. (Companion work to Basic Facts of Medical Microbiology.) 79 pages; 85 figures. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $2.

BASIC FACTS OF MEDICAL MICROBIOLOGY, by *Stewart M. Brooks,* M. S. 306 pages; 122 figures. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $4.75.

THE CHEMISTRY OF BLOOD COAGULATION, by *Paul Morawitz,* Marburg, Germany. Translated by *Robert C. Hartmann,* M. D., and *Paul F. Guenther,* M. A., Ph. D. American Lecture Series, Publication No. 314, A Monograph in the Bannerstone Division of American Lectures in Hematology, edited by *Frank H. Bethell,* M. D. 194 pages. Charles C Thomas, Publisher. Springfield, Ill., 1958. Price $4.50.

PARENT-CHILD TENSIONS, by *Berthold Eric Schwarz,* M. D., and *Bartholomew A. Ruggieri,* M. D. 238 pages. J. B. Lippincott Co., Philadelphia, Pa., 1958. Price $4.95.

AMERICAN DRUG INDEX, 1958, by *Charles O. Wilson,* Ph. D., and *Tony Everett Jones,* Ph. D. 716 pages. J. B. Lippincott Co., Philadelphia, Pa., 1958. Price $5.

NURSING IN DISEASES OF THE EYE, EAR, NOSE AND THROAT, from the *Manhattan Eye, Ear and Throat Hospital.* 10th edition. 269 pages; 83 illustrations. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $4.50.

REACHING DELINQUENTS THROUGH READING, by *Melvin Roman,* Ph. D. American Lecture Series, Publication No. 313, A Monograph in The Bannerstone Division of American Lectures in Psychology, edited by *Molly Harrower,* Ph. D. 125 pages. Charles C Thomas, Publisher, Springfield, Ill., 1957. Price $4.50.

5-HYDROXYTRYPTAMINE, Proceedings of a Symposium held in London on 1 and 2 April, 1957, edited by *G. P. Lewis,* Ph. D. 253 pages; illustrated. Pergamon Press, New York, N. Y., 1958. Price $9.50.

NEW AND NONOFFICIAL DRUGS, Containing descriptions of therapeutic, prophylactic and diagnostic agents evaluated by The Council on Drugs (Formerly, Council on Pharmacy and Chemistry) of The American Medical Association. 645 pages. J. B. Lippincott Co., Philadelphia, Pa., 1958. Price $3.35.

THE YEAR BOOK OF THE EAR, NOSE AND THROAT AND MAXILLO-FACIAL SURGERY (1957-1958 Year Book Series). The Ear, Nose and Throat, edited by *John R. Lindsay,* M. D. Maxillofacial Surgery, edited by *Dean M. Lierle,* M. D., and *William C. Huffman,* M. D. 383 pages; illustrated. The Year Book Publishers, Inc., Chicago 11, Ill., 1958. Price $7.50.

PHYSICAL DYNAMICS OF CHARACTER STRUCTURE, Bodily Form and Movement in Analytic Therapy, by *Alexander Lowen,* M. D. 358 pages; illustrated. Grune and Stratton, Inc., New York, N. Y., 1958. Price $7.75.

MEDICINE AND MAN, The Story of the Art and Science of Healing, by *Ritchie Calder.* 256 pages. A Mentor Book published by The New American Library of World Literature, Inc., New York 22, N. Y., 1958. Price $0.50.

POLYSACCHARIDES IN BIOLOGY, Transactions of the Second Conference, April 25, 26, and 27, 1956, Princeton, N. J., edited by *Georg F. Springer,* M. D. 245 pages; illustrated. Josiah Macy, Jr. Foundation, New York, N. Y., 1958. Price $5.

GROUP PROCESSES, Transactions of the Third Conference, October 7, 8, 9, and 10, 1956, Princeton, N. J., edited by *Bertram Schaffner,* M. D. 328 pages; illustrated. Josiah Macy, Jr. Foundation, New York, N. Y., 1958. Price $4.

HEALTH FACTS FOR COLLEGE STUDENTS, A Textbook of Individual and Community Health, by *Maude Lee Etheredge,* M. D., Dr. P. H. Foreword by *Ray Lyman Wilbur,* M. D. 412 pages; illustrated. Published by W. B. Saunders Co., Philadelphia, Pa., 1958. Price $4.75.

FUNDAMENTALS OF NEUROLOGY, by *Ernest Gardner,* M. D. 3d edition. 359 pages; illustrated. Published by W. B. Saunders Co., Philadelphia, Pa., 1958. Price $4.75.

HEALTH TEACHING IN SCHOOLS, For Teachers in Elementary and Secondary Schools, by *Ruth E. Grout,* M. P. H., Ph. D. 3d edition. 359 pages; illustrated. Published by W. B. Saunders Co., Philadelphia, Pa., 1958. Price $4.75.

NON-VENEREAL SYPHILIS, A Sociological and Medical Study of Bejel, by *Ellis Herndon Hudson,* M. D., D. T. M. & H. (Lond.), F. A. C. P. 204 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., 1958. Price $7.

DYNAMICS OF PSYCHOTHERAPY, The Psychology of Personality Change, by *Percival M. Symonds,* Ph. D. Volume III, Procedures. 634 pages. Grune and Stratton, Inc., New York, N. Y., 1958. Price $6.50.

A GUIDE TO HUMAN PARASITOLOGY FOR MEDICAL PRACTITIONERS (*Blacklock* and *Southwell*), Revised by *T. H. Davey,* O. B. E., M. D., D. T. M. Sixth Edition. 222 pages; with three colored plates and 119 illustrations. The Williams and Wilkins Co., Baltimore, Md., 1958. Price $7.

VETERINARY ANAESTHESIA, by *John G. Wright.* 4th edition. 317 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., 1957. Price $6.75.

CIBA FOUNDATION SYMPOSIUM ON THE CHEMISTRY AND BIOLOGY OF MUCOPOLYSACCHARIDES, edited by *G. E. W. Wolstenholme,* O. B. E., M. A., M. B., B. Ch., and *Maeve O'Connor,* B. A. 323 pages; 48 illustrations. Little, Brown and Company, Boston, Mass., 1958. Price $8.50.

AN INTRODUCTION TO EXPERIMENTAL SURGICAL STUDIES, by *W. J. Dempster,* F. R. C. S. 463 pages; illustrated. Charles C Thomas, Springfield, Ill., 1958. Price $10.

A MANUAL OF ELECTROTHERAPY, by *Arthur L. Watkins,* M. D. 259 pages; 167 illustrations and 1 plate in color. Lea & Febiger, Philadelphia, Pa., 1958. Price $5.

THE IMPACT OF THE ANTIBIOTICS ON MEDICINE AND SOCIETY, Monograph II, Institute of Social and Historical Medicine, The New York Academy of Medicine. Edited by *Iago Galdston,* M. D. 222 pages. International Universities Press, Inc., New York, N. Y., 1958. Price $5.

CHRONIC SCHIZOPHRENIA, by *Thomas Freeman,* M. D., D. P. M.; *John L. Cameron,* M. B., CH. B., D. P. M.; and *Andrew McGhie,* M. A. Preface by *Anna Freud.* Foreword by *T. Ferguson Rodger.* 158 pages. International Universities Press, Inc., New York, N. Y., 1958. Price $4.

ROENTGENOLOGY OF THE CHEST, edited by *Coleman B. Rabin,* M. D., F. C. C. P. 484 pages; illustrated. Charles C Thomas, Springfield, Ill., 1958. Price $19.50.

HIGH ARTERIAL PRESSURE, by *F. H. Smirk,* M. D., F. R. C. P., F. R. A. C. P. 764 pages; illustrated. Charles C Thomas, Springfield, Ill., 1958. Price $15.

FAT CONSUMPTION AND CORONARY DISEASE: THE EVOLUTIONARY ANSWER TO THIS PROBLEM (A basic approach to the prevention and arrest of coronary disease), by *T. L. Cleave,* M. R. C. P. (Lond.). Foreword by *Percy Stocks,* C. M. G., M. A., M. D., F. R. C. P., F. S. S. 40 pages. Philosophical Library, New York, N. Y., 1958. Price $2.50.

VIRAL ENCEPHALITIS, A Symposium, Fifth Annual Scientific Meeting of the Houston Neurological Society, Texas Medical Center, Houston, Tex. Compiled and edited by *William S. Fields* and *Russell J. Blattner.* 225 pages; illustrated. Charles C Thomas, Springfield, Ill., 1958. Price $7.

AN INTRODUCTION TO PHARMACOLOGY AND THERAPEUTICS, by *J. A. Gunn*, C. B. E., M. A., M. D., D. Sc., F. R. C. P., with the assistance of *J. D. P. Graham*, B. Sc., M. D., F. R. F. P. S., F. R. C. P. 9th edition. 329 pages. Oxford University Press, New York, N. Y., 1958. Price $4.25.

THE YEAR BOOK OF OPHTHALMOLOGY (1957-1958 Year Book Series), edited by *Derrick Vail*, B. A., M. D., D. Oph. (Oxon.), F. A. C. S., F. R. C. S. (Hon.) 423 pages; illustrated. The Year Book Publishers Inc., Chicago, Ill., 1958. Price $7.50.

CONNECTIVE TISSUE, A Symposium organized by The Council for International Organizations of Medical Sciences, Established under the Joint auspices of UNESCO and WHO. Edited by *Madeline Keech*, *J. F. Delafresnaye*, and *G. C. Wood*, under the direction of *R. E. Tunbridge*. 371 pages; illustrated. Charles C Thomas, Publisher, Springfield, Ill., 1958. Price $8.50.

HEART DISEASE IN INFANCY AND CHILDHOOD, by *John D. Keith*, M. D., *Richard D. Rowe*, M. D., F. R. C. P., and *Peter Vlad*, M. D. 877 pages; illustrated. The Macmillan Company, New York, N. Y., 1958. Price $22.50.

OUR NUCLEAR ADVENTURE, Its Possibilities and Perils, by *D. G. Arnott*. 170 pages; illustrated. Philosophical Library, New York, N. Y., 1958. Price $6.

THE ATOMIC AGE AND OUR BIOLOGICAL FUTURE, by *H. V. Brondsted*. Translated by *E. M. Huggard*. 80 pages. Philosophical Library, New York, N. Y., 1958. Price $2.75.

THE DRUG–THE NURSE–THE PATIENT, by *Mary W. Falconer*, R. N., M. A., and *Mabelclaire Ralston Norman*, R. N., B. S. 631 pages; illustrated by *Marian S. Rosenbloom*. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $5.75.

RAND, SWEENY AND VINCENT'S GROWTH AND DEVELOPMENT OF THE YOUNG CHILD, by *Marian E. Breckenridge*, M. S., and *Margaret Nesbitt Murphy*, Ph. D. Sixth Edition. 548 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $5.50.

CURRENT DRUG HANDBOOK, by *Mary W. Falconer*, R. N., M. A., and *H. Robert Patterson*, B. S., M. S., Pharm. D. 157 pages. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $3.25.

GENERAL ZOOLOGY, by *Claude A. Villee*, *Warren F. Walker, Jr.*, and *Frederick E. Smith*. 877 pages; 444 illustrations. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $7.50.

LABORATORY EXERCISES IN GENERAL ZOOLOGY, by *Harvey I. Fisher*, Ph. D., and *James B. Kitzmiller*, Ph. D. 227 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $4.

THE TREATMENT OF FRACTURES, by *Lorenz Bohler*, M. D. Volume III. Translated from the Thirteenth German Edition by *Alfred Wallner*, M. D., and *Otto Russe*, M. D. 2,307 pages; 1699 illustrations. Grune and Stratton, Inc., New York, N. Y., 1958. Price $21.

RESEARCH IN NURSING, by *Amy Frances Brown*, R. N., B. Ed., M. S. in N., Ph. D. 352 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., 1958. Price $5.75.

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